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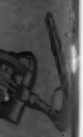

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REFLUX ESOPHAGITIS.*

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Until recent times, little attention has been given to an inflammatory condition of the lower portion of the esophagus, now designated reflux or peptic esophagitis. The otolaryngologist has been well versed in the diagnosis and treatment of chemical burns and resultant stenotic lesions of the esophagus but has manifested less familiarity with other etiologic factors of esophagitis.

Winkelstein,[54] in 1935, described a "new clinical entity," which he named peptic esophagitis. Noting a relationship between acute esophagitis and peptic ulcer of the stomach and duodenum, he ascribed the inflammation of the esophagus in such cases to the action of pepsin and hydrochloric acid on a susceptible mucosa. There is a high degree of susceptibility of the nonresistant squamous mucosa of the esophagus to prolonged contact with gastric and intestinal secretions. Other causes of peptic esophagitis are regurgitation accompanying vomiting, and reflux of gastric contents because of some impairment of the sphincter-like action of the cardioesophageal junction associated with sliding hiatal hernia or the surgical excision of the cardiac sphincter. The term reflux esophagitis, introduced by Allison,[1] accurately describes this entity; also it seems preferable to peptic esophagitis, because peptic carries the connotation of association with ulcer of the stomach and duodenum.

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Esophagitis is the lesion most frequently encountered in the esophagus;[33] nevertheless, it has not received the attention it deserves in medical literature.[32] From a clinical standpoint, the esophagus has remained shrouded in mystery. In the opinion of Vinson,[35] the gastroenterologist has been too prone to consider the esophagus outside his diagnostic domain, and the otolaryngologist too frequently has limited his study of this organ to inspection through an esophagoscope. In addition, there has been a tendency to permit the roentgenologist to rule out organic disease of the esophagus, and diagnostic esophagoscopy has been a neglected procedure.[33] Recently, however, the literature has reflected increasing interest in this organ.

The purpose of this presentation is to discuss the subject of reflux esophagitis with regard to anatomy and physiology, pathology, symptoms, diagnosis, etiology as illustrated by specific cases, and treatment. Study of this disease and experience in dealing with its manifestations, as demonstrated by the cases reported, indicate the importance of creating an awareness of this entity, for it appears to be more prevalent than is generally realized.

ANATOMY.

Of Greek derivation, the term esophagus means to carry food, a definition which explains the main function of the musculomembranous tube extending from the lower border of the pharynx to the stomach. This tube originates at the level of the lower border of the cricoid cartilage opposite the sixth cervical vertebra and enters the stomach and the abdomen at the level of the tenth thoracic vertebra. The average length of the adult esophagus is 10 inches. The respective layers of the esophagus from within out are the mucosa, lamina propria mucosae, muscularis mucosae, submucosa, muscularis propria, and adventitia. The mucous membrane lining is made up of stratified squamous epithelium. Food passes through the esophagus with great rapidity. There is no need here for an absorptive or digestive role.[46] The lining epithelium's main function is that of a protective coating. Since no absorption occurs, there is little need for lymphatic tissue

to filter any tissue fluid. Small amounts of lymphatic tissue are present, however, in areas where ducts or glands pass through the lamina propria.[46] The transition from the stratified squamous epithelium to the gastric epithelium is histologically abrupt.[33]

There are two types of esophageal glands: the deep or true esophageal mucous glands have a sparse and uneven distribution over the length of the esophagus. There are seldom more than 200 mucous glands in the human esophagus, and about two-thirds of these occur in the upper half.[33] These glands lie in the submucosa, and each has a single secretory duct lined with stratified squamous epithelium. The superficial or esophageal cardiac glands lie in the mucosa. They are morphologically similar to gastric cardiac glands. Most of these are concentrated between the level of the cricoid cartilage and the fifth tracheal ring and the distal few millimeters of the esophagus. Palmer[33] believed that the histologic similarity of the normal esophageal cardiac glands to the gastric cardiac glands accounts for some confusion in the literature regarding the diagnosis of heterotopic gastric mucosa in the esophagus. In his opinion, the diagnosis of the abnormal state must depend on the identification of both gastric parietal and chief cells in the tissue questioned.

The muscularis propria consists of an outer longitudinal layer and an inner circular layer. It is composed of both smooth and striated muscle. The latter extends down to the middle of the esophagus; the remaining portion is made up of smooth muscle fibers.

The nerve supply is derived from the sympathetic and parasympathetic nervous system. The sympathetic fibers are supplied through the cervical and thoracic parts of the sympathetic chain, and the parasympathetic fibers are supplied through the vagus and recurrent laryngeal nerves. The intrinsic nerve plexus of Meissner and that of Auerbach are present in the esophagus; the former in the submucosal layer and the latter between the inner and outer muscle layers.

The Terminal Portion of the Esophagus.—A review of the literature indicates wide diversity of opinion regarding the

anatomy and physiology of the terminal portion of the esophagus. There is also disagreement as to the presence of a true sphincter at the gastroesophageal junction.

In the cadaver the gastroesophageal junction lies opposite the tenth or eleventh cervical vertebra. During life its position is variable because of the excursions of normal diaphragmatic movements.

The diaphragm is a muscular sheet composed of fibers radiating from the lower border of the thorax and from the upper lumbar vertebrae toward a central tendinous area. These muscle fibers are grouped into three portions according to their origin: the sternal, costal, and lumbar. The two crura which form the hiatus for the esophagus arise from the lumbar portion. Behind the posterior margin of the central tendon, the crural fibers diverge to surround in a sphincter-like manner the hiatus for the esophagus. Mosher[25] demonstrated that the anterior or right crus is thin and may be membranous. The posterior crus is sturdy; it makes a prominent crease on the posterior surface of the esophagus and notches its left border. In his opinion the form of the crural sling varies and with it the form of the terminal portion of the esophagus. He divided this portion of the esophagus into a vertical and horizontal arm. This division is due to a twist of the esophagus on itself from right to left at the crura of the diaphragm. This author observed a close relationship between the lower segment of the esophagus and the liver and believed the latter responsible for the shape of the lower end of the esophagus.

Palmer[33] noted that the esophagogastric junction lies immediately anterior to the medial border of the spleen. Mosher[25] stated that the horizontal arm of the terminal portion of the esophagus is imprisoned between the posterior crus and the posterior surface of the liver in front. The anterior crus comes in between the liver and the horizontal arm in front. He concluded that to and fro movements of the liver will open and close the horizontal portion of the lower part of the esophagus and that its patency is controlled by the position of the liver. It was his belief that the terminal portion of the esophagus is closed during the resting state because of the pressure in the crural canal, the pressure of the deep vertical

folds, and the natural twist to the left; also that a weak sphincter can be demonstrated occasionally at the lower end of the esophagus. He noted a thickening of both muscular layers of the esophageal wall at the line where the esophageal mucosa changes into gastric mucosa, which he considered to be a cardiac sphincter. It was his conclusion that a cardiac sphincter is not always present, and in five out of seven of his dissections he observed that the esophageal muscles came to a definite ending at the level of the crura and did not reach the cardia. In his opinion the musculature of the lower end of the esophagus or upper end of the stomach has a weak sphincteric action regardless of the presence or absence of an anatomic sphincter.

Fig. 1a. The right crus of the diaphragm forming a sling for the esophagogastric junction. Anterior view. b. The sling of the right crus as seen from the side. Redrawn from Allison.[2]

According to Allison,[1] the cardia allows food to pass from the esophagus to the stomach and prevents the reflux of digestive juices from the stomach into the esophagus. There is no thickening of circular muscle fibers of the esophagus to form a sphincter. The esophagus bends forward and to the left, and this bend is lassoed and maintained by the right crus of the diaphragm, which hitches it down to the lumbar spine (see Fig. 1). The esophageal hiatus is a split in the muscle fibers of the right crus, which is tightly reinforced by fibers from the left. The esophagus is supported in front by a sling of muscle fibers continuous on each side with the perpendicular fibers of the crus and decussating with one another to form a stoutly reinforced raphe. There is less support behind, because

the crus splits here to form the hiatus. Pressure from below at this point splits the fibers to increase the size of the opening. When the right crus of the diaphragm contracts, it compresses the walls of the esophagus from side to side and pulls down and increases the angulation of the esophagus, both from before backward and from side to side. It is during inspiration when the suction pressure in the chest would tend to draw the gastric contents into the esophagus that the crus of the diaphragm contracts and prevents this reflux. In addition to making these observations, this author concluded that no internal sphincter can be demonstrated. He believed that there is an intrinsic mechanism which contributes to continence. Part of this mechanism is the oblique line of entry of the esophagus into the stomach and contraction of the circular muscle fibers of the esophagus and the oblique fibers of the stomach. Carver and Sealy[10] believed that the contraction of these muscles produces a purse-string action. They suggested that air in the cardia produces a pressure effect which tends to collapse the esophagus and increase the esophagocardiac angle.

Lerche[27] studied in cadavers the closing mechanism between the stomach and esophagus which he believed had been active in a phase of regurgitation of stomach contents at the time of death. He concluded that there is a double closing mechanism between the stomach and esophagus. The structures involved in this mechanism were considered by him as a unit which he labeled "the gastroesophageal segment of expulsion." This unit consists of (*1*) the phrenoesophageal elastic membrane, (*2*) the ampulla, (*3*) the inferior esophageal sphincter, (*4*) the gastroesophageal vestibule, and (*5*) the constrictor cardiae.

The phrenoesophageal elastic membrane originates from the fascia of the diaphragm, enters both muscle layers at the lower end of the esophagus and terminates in the inferior esophageal sphincter above the diaphragm. There is a descending portion which covers the subhiatal fat ring. This membrane maintains proper relationship between the esophagus, the diaphragm, and the stomach. It restrains excessive shortening of the esophagus during the contraction of the

longitudinal muscle layer and serves as a barrier against intra-abdominal pressure. Lerche[27] believed that the esophagus terminates above the hiatus of the diaphragm in the ampulla, the lower end of which is always closed by the inferior esophageal sphincter, which is always in tonic contraction except during the passage of contents. The ampulla is a dilatation of the lower portion of the esophagus which is only discernible after food has been introduced. He described it as 1.5 to 2 cm. in length and varying in shape with the state of contraction of its musculature.

The inferior esophageal sphincter, according to this author, is a circumscribed thickening of the muscular wall above the hiatus of the diaphragm. This sphincter is always closed in tonic contraction, and in his opinion it is the only closure between the negative pressure of the esophagus and the positive pressure in the stomach. In a large number of the specimens, this was 1 to 2 cm. above the diaphragmatic hiatus. The thickness of the muscle varied greatly, in many specimens from 3 to 5 mm. In a few cases there was no difference in thickness of the muscle wall here and elsewhere in the esophagus. He concluded that the thickness depends upon the state of contraction of the muscle.

The gastroesophageal vestibule is a dilatation between the inferior esophageal sphincter above and the constrictor cardiae below. The constrictor cardiae consists of a right and left sling of muscle fibers which form a circular muscle ring during contraction.

Lerche[27] described the passage of food from the terminal end of the esophagus to the stomach as follows: after the bolus enters the ampulla, the esophageal sphincter opens mechanically or reflexly to the peristaltic pressure above the ampulla. The inferior esophageal sphincter then contracts and forces the bolus into the gastroesophageal vestibule. When the latter is filled, the inferior esophageal sphincter closes, and the constrictor cardiae opens as the vestibule shortens by contraction of the deep longitudinal muscle layer which pulls it to the sphincter. The contents are then introduced into the stomach through the orifice of the constrictor cardiae. He believed that the constrictor cardiae functions as

an adjustable mouthpiece which controls the pressure in the vestibule and the passage of swallowed material of varying consistency. After the expulsion of the contents, the constrictor cardiae projects into the stomach, and the gastroesophageal vestibule extends with it. The constrictor cardiae relaxes, and the mucosa of the vestibule everts into the stomach (see Fig. 2).

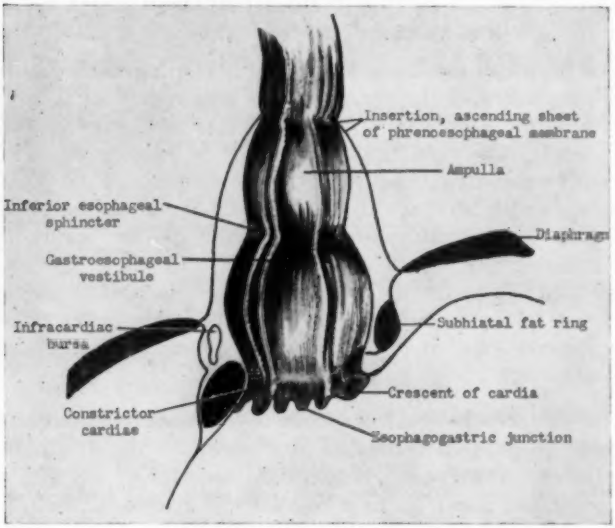

Fig. 2. The gastroesophageal segment of expulsion, as described by Lerche. Redrawn from Palmer.[33]

Templeton[44] stated that roentgenologic observations on man indicate the presence of both a sphincter inherent in the walls of the lower portion of the esophagus and a pinchcock action which plays a part in closing the terminal portion of the esophagus.

PATHOLOGY.

Early acute ulcerative esophagitis is manifest in the esophagus by patchy superficial erosion, surface exudate, and hyperemia of the involved portions with or without petechiae.

The distal portion is affected in almost all cases, and in approximately two thirds this segment alone is involved.[33] Small oval erosions are distributed in longitudinal streaks. Bartels,[3] in 1935, found evidence of ulcerative esophagitis in 82 of 6,000 fresh and preserved esophageal specimens, an incidence of 0.013 per cent. In all of these specimens the esophagus was dilated, especially the lower third.

The incidence of esophagitis in the esophageal specimens of 3,032 necropsies, examined by Butt and Vinson[9] in 1936, was 7.02 per cent. In 76.5 per cent of the 213 cases of esophagitis in this series the lesions were of the acute ulcerative type. There was a denuding of the lining epithelium. The inflammatory reaction, varying from mild to severe, involved the submucosa and both layers of muscle. Polymorphonuclear leukocytes predominated. Hemorrhage was evident in the various layers. The mucous glands were inflamed, and the ducts blocked and dilated. Vessels dilated and engorged with erythrocytes were present in the submucosa. A ruptured vessel occasionally was seen in the lumen of the esophagus, and thrombosed vessels and lymphatic vessels filled with leukocytes were also observed occasionally. A subacute process manifest by a denuding of the epithelial layer and an infiltration with leukocytes was observed in 31, or 14.5 per cent, of the cases. Beginning fibroblastic proliferation was present. In 14, or 6.5 per cent, of the cases a chronic process was indicated by replacement of most of the muscularis mucosae and submucosa with fibrous tissue. The thickness of the subepithelial connective tissue was appreciably increased. These authors believed the areas of fibrosis represented the result of repeated attacks of esophagitis with healing. Accompanying the increased fibrosis was a diminished blood supply to the mucous membrane, which decreased the normal resistance of this tissue. This change, in their opinion, probably facilitated recurrent attacks of esophagitis.

Inflammatory change may penetrate the walls of the esophagus deeply enough to produce a stricture of this organ with resultant dysphagia within a month or two of the time of the onset of the inflammatory process.[48] The progressive course of an untreated acute ulcerative esophagitis is chronic

ulceration, fibrosis, and benign stricture formation.[1,6,10,11,20,26,37,48] As in the stomach and duodenum, this course may be complicated by bleeding or perforation.

SYMPTOMS.

The symptoms of reflux esophagitis vary from bizarre thoracic pain to pronounced dysphagia and hemorrhage. In a patient of the psychoneurotic type, probably too often the early symptoms are considered functional in nature and are disregarded by the physician. Butt and Vinson[9] noted definite clinical symptoms in only 10.3 per cent of 213 patients. Substernal burning and pain, hematemesis, and dysphagia were the most common symptoms in their series, and obstruction was a late symptom. Symptoms listed by Carver and Sealy[10] were substernal pain, nausea, regurgitation, vomiting, dysphagia, aphagia, hematemesis, and melena. Characteristically, they observed, these symptoms occur either alone or in various combinations according to the stage of the disease. The earliest symptom is usually substernal pain, often described as "heartburn," which at first is transient and promptly relieved by ingestion of bland food or antacids. The pain increases in severity as the disease progresses and may persist for several hours after meals without relief after the swallowing of antacids or bland food. It may radiate to the head, neck, or back, or down the arm as in acute coronary insufficiency. These authors explained the radiation of the pain on the basis of the sympathetic and parasympathetic innervation of the esophagus, which is cervical, thoracic, and vagal in origin and similar to the innervation of the heart. As the disease progresses, dysphagia results from muscle spasm and edema. Later ulceration occurs, resulting in fibrosis, cicatricial stenosis, and shortening of the esophagus.

Loss of weight and anemia are frequently associated findings. Patients dread swallowing so much that they refuse to eat, or soon find they can take only a liquid diet, for to ingest solid food is to risk complete obstruction. Regurgitation of saliva, especially before arising in the morning, is a distressing symptom. Also, in almost all cases occult blood is demonstrable in the stool, with severe hematemesis and melena occurring in about 10 per cent of the cases.[9]

DIAGNOSIS.

The diagnosis of reflux esophagitis depends first on the recognition of the symptoms. Vague symptoms of fulness in the chest and choking sensations associated with retrosternal burning deserve prompt evaluation and should not be discarded as functional complaints. A carefully taken history should be followed by Roentgen examination of the gastrointestinal tract. The differential diagnosis should exclude angina pectoris, cholecystitis, peptic ulcer of the stomach or duodenum, carcinoma of the esophagus, true cardiospasm, and peptic ulceration of the thoracic stomach.[4] The roentgenologist should be informed of the history and of the possibilities of reflux esophagitis when the patient is referred to him. He then may look carefuly for evidence of sliding hernia, gastric reflux, or other abnormalities of the lower portion of the esophagus.

The sphincteric action of the cardia prevents regurgitation of barium into the esophagus when the normal subject lies in the Trendelenburg position. Regurgitation of barium from the cardia into the esophagus occurs in subjects suffering from cardioesophageal reflux. The regurgitation may fill only the lower end of the esophagus or may fill the esophagus as far as the mouth.[32] Samuel [38] advised a careful search for signs of reflux esophagitis in patients showing cardioesophageal reflux, for it does not occur in all such patients. Other Roentgen findings in reflux esophagitis are spasm of the esophagus, irregularity of the mucosal contours, and stenosis. An ulcer crater niche may be demonstrated in peptic ulcer of the esophagus secondary to reflux esophagitis. Care should be exercised in differentiating esophageal carcinoma from reflux esophagitis.

Hiatal hernia with or without spasm or stricture above is the most common Roentgen finding in this disease.[4] The Roentgen diagnosis of hiatal hernia and shortened esophagus is important. Dawson[12] described the difficulty in differentiating an epiphrenic ampulla from a hiatal hernia. A positive Roentgen diagnosis of hiatal hernia should not be made unless it is demonstrated that reflux and filling of the hiatal hernia are spontaneous from a barium-filled stomach. His method is to fill the stomach with barium with the patient in the erect position and then to tilt the patient into the Trendelenburg

position to produce reflux of barium into the hiatal hernia. Should this procedure fail to demonstrate a hiatal hernia, the patient stands in the erect lateral position and bends to touch his toes. If the hiatus is incompetent, a hiatal hernia of the stomach will bulge above the diaphragm.

Esophagoscopy should be performed in patients with Roentgen evidence of esophagitis. The persistence of esophageal symptoms in the absence of positive Roentgen findings still requires esophagoscopic examination. Carcinoma must be differentiated from stricture formation in the late stages of reflux esophagitis. Repeated esophagoscopies and biopsies are necessary in suspicious cases. The specimen for biopsy should be taken from the deep layers of the esophagus. The esophagoscopic findings vary with the stage of the disease. In acute reflux esophagitis, the mucosa is diffusely edematous and inflamed. Small ulcers with whitish exudate may be present; the exudate is readily stripped off, leaving a bleeding surface. There may be a discrete ulcer with an inflammatory reaction. Spasm of the esophagus may or may not be present in the early stages. In later stages stricture formation occurs with pronounced narrowing of the lumen. The mucosa is usually friable and bleeds easily with manipulation. The presence of a shortened esophagus with a hiatal hernia may be established. This condition is usually accompanied by an incompetent cardia, which facilitates the entrance of the esophagoscope into the stomach. The usual narrowing and bending of the lower portion of the esophagus are absent in cases of this type.

ETIOLOGY.

Regurgitation of gastric contents in infants is a normal occurrence. The muscles of the diaphragm strengthen with age and contribute to the normal function of the closing mechanism of the cardioesophageal function. In a study of 310 autopsies in infants, Gruenwald and Marsh[21] noted evidence of acute esophagitis usually with ulceration in one out of every six infants. The most common localization of esophageal ulcers was just above the cardia. Inflammation ended abruptly where gastric mucosa began. These authors believed that ob-

stetric complications and severe asphyxia predispose an infant to esophagitis. Five of six infants with kernicterus had esophagitis. Perforation of an esophageal ulcer into the pleural cavity occurred in two cases. They suggested that in many of the cases the lesions were "shock lesions." Anoxia and severe dehydration with resultant hemoconcentration were the suggested causes of shock. Vomiting occurred in 34 of the 52 cases in the series, and the vomitus contained blood in 17. The diagnosis of esophagitis is strongly suggested when an infant vomits blood.

Beaconsfield[4] noted that spasm and fibrosis of the circular muscle fibers produce stenosis, while spasm or fibrosis of the longitudinal muscle fibers shortens the esophagus. The shortening of the esophagus impairs the function of the cardiac sphincter. He described a vicious cycle of inflammation, fibrosis, constriction, and contraction producing stricture and shortening of the esophagus, drawing up the stomach into the thoracic cavity and increasing the size of the hiatal hernia, which in turn favors the regurgitation of the gastric contents into the esophagus.

Most authors mention a close relationship between esophagitis and other diseases of the gastrointestinal tract, especially those in which there is frequent vomiting or regurgitation of gastric secretions.

Bartels[3] reported gastric contents in all of his cases of ulcerative esophagitis, and the flow between the stomach and the esophagus was uninterrupted. He observed no ulceration in cases in which the esophagus was firm with normal folding rugae present.

Mechanical factors of stretching and the act of regurgitation may cause small breaks in the esophageal mucosa which, when bathed by gastric secretion, tend to produce congestion and erosion of the membrane.[26]

Selye[41] was able to produce hemorrhagic esophagitis by ligating the pylorus in animals, thus showing that prolonged contact between esophageal mucosa and gastric juice resulted in inflammation.

Also by animal experimentation, Ferguson and his associ-

ates[16] demonstrated that contact of gastric juice with esophageal mucosa had a devastating effect. It was much less damaging on intestinal mucosa. Perfusion of a cat's esophagus with canine gastric juice resulted in a perforation of the esophagus in 19 minutes in one animal. The lower third of the esophagus was always most severely damaged. Hydrochloric acid alone in a similar concentration to that in gastric juice had a mild effect on the esophagus. When bile and pancreatic secretion were added to the gastric juice being applied, little damage occurred to the esophagus. These investigators concluded that peptic activity is the important factor and that prevention and treatment of ulcerative esophagitis should be directed toward preventing reflux of gastric juice into the esophagus.

The roentgenologist frequently sees Roentgen evidence of a reflux of barium from the stomach to the esophagus in the normal person. In summarizing a review of the literature on regurgitation, Butt and Vinson[8] concluded that the strongest evidence favors the theory that regurgitation of gastric content into the esophagus occurs as a normal process in a high percentage of cases. It was their opinion that the esophageal mucosa is a well protected membrane. Mucus secreted by the esophageal, nasal and pharyngeal glands forms a continuous blanket protecting the membrane lining of the esophagus. They concluded that it is only when there is an inadequate amount of mucus present or when the membrane is injured in some way that the regurgitated gastric juice plays an important role in the production of ulcerative esophagitis.

Indwelling feeding and suction tubes may be an etiologic factor in reflux esophagitis. Trauma to the esophageal mucosa by these tubes may make it more susceptible to the reflux of gastric juice. The indwelling tube may straighten partially the kinking of the lower portion of the esophagus and encourage the gastric reflux. Benedict and Gillespie[5] suggested that patients requiring prolonged intubation are those more likely to vomit and have gastric reflux with or without the indwelling tube. The danger of peptic digestion with indwelling stomach tubes is particularly high in patients suffering from prolonged debility or unconsciousness.[38] In 20 per cent of the cases reported by Butt and Vinson[9] there was associated

peptic ulcer of the stomach or duodenum, and in half of these cases the patient had vomited or had had gastric contents removed by tube, or both.

Postoperative Reflux Esophagitis.—Two cases are described which illustrate the occurrence of reflux esophagitis following cholecystectomy. In Case 1 an indwelling tube and vomiting postoperatively were factors, and in Case 2 reflux of gastric content was among the suggested etiologic factors.

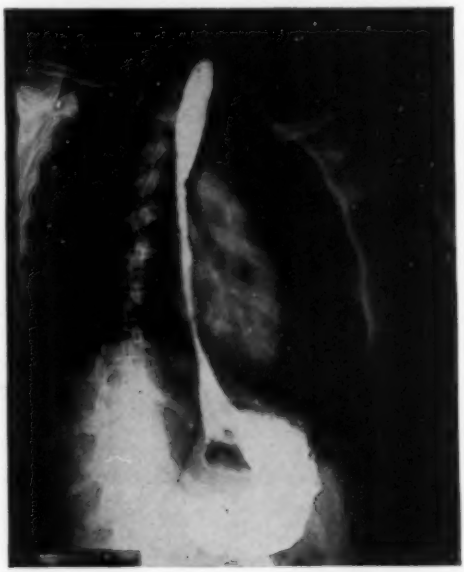

Fig. 3. Case 1.—Roentgenogram showing narrowing and irregularity of the lower two thirds of the esophagus on Nov. 22, 1952.

Case 1. J. H. W., a white woman, aged 64, complaining of dysphagia, was referred by an internist on Dec. 11, 1952. For several months prior to cholecystectomy on the preceding August 16, recurrent episodes of upper abdominal discomfort associated with nausea and occasional vomiting had increased in severity. There was Roentgen evidence preoperatively of several stones in the gallbladder, but the esophagus and stomach were normal in appearance. For four days after uneventful cholecystectomy a Levin tube was left in place. On the fourth postoperative day severe and persistent vomiting occurred and continued intermittently for three weeks. Following discharge from the hospital on the forty-sixth post-

operative day, the patient was seen at home by her physician on several occasions because of recurrent symptoms of esophageal spasm manifested by a stoppage of food at the manubrial level. She experienced frequent regurgitation of food and liquids and complained of substernal pain radiating to the neck and back. A barium swallow on September 18 demonstrated a normal-appearing esophagus, but on November 22 a second examination by barium swallow gave evidence of narrowing and irregularity of the lower two-thirds of the esophagus (see Fig. 3). Gastric analysis before and after administration of histamine demonstrated gastric acidity to be within normal limits.

Fig. 4. Case 1.—Roentgenogram showing advanced esophageal narrowing on March 26, 1954, 16 months later.

On esophagoscopy, one week after the patient first consulted me, the mucosa of the esophagus had an edematous appearance throughout with retained greenish secretions present in the upper portion. At a point 25 cm. from the upper alveolus, the esophagus narrowed markedly, and the very red, acutely inflamed tissue bled easily upon manipulation. The diagnosis was acute esophagitis. The report on the histopathologic examination of the specimen taken for biopsy was a granulomatous inflammatory process with necrotic tissue.

For six weeks thereafter it was possible to pass a No. 16 French Hurst dilator, although dilatation was especially difficult because of pain, nausea and apprehension. On March 5, 1953, it became necessary to resort to gastrostomy, and retrograde dilatations were carried out until June 2, when the gastrostomy was closed. At the time of closure a No. 38 French Tucker retrograde dilator was in use, and dilatations from above were

easily carried out with a No. 24 French Hurst dilator. Dilatations with the Hurst dilator were continued until September. Gradual narrowing of the esophagus then recurred. When it was possible to use only a No. 16 French Hurst dilator, dilatation over a string was begun and is still being continued, with the Hurst dilator being used intermittently. There have been 84 dilatations to date, and a No. 27 French dilator is now employed.

On March 23, 1954, esophagoscopy was repeated. The upper portion of the esophagus appeared normal. Thirty centimeters from the upper alveolus, the esophagus narrowed markedly; the mucous membrane was greatly inflamed and upon manipulation bled easily. Roentgen examination three days later demonstrated a slightly dilated upper portion of the esophagus with tapering at the level of the seventh and eighth dorsal vertebrae and stricture formation at the ninth dorsal vertebra (see Fig. 4). This area appeared to be seven inches in length. There was a lack of peristalsis throughout the lower half of the esophagus.

Comment.—This case illustrates an acute reflux esophagitis progressing through the chronic phase to stricture formation apparently due to severe vomiting following surgery. The persistence of the activity for two years is noteworthy. Dilatation over the string until recently has been very painful with pain radiating to the back and neck, and has frequently been followed by slight bleeding. The persistent activity probably has been due to continued reflux of gastric juice into the acutely inflamed esophagus. The patient has been most resistant to any suggestion of possible surgery to alleviate this problem. At present the dilatations are at monthly intervals with a No. 27 French dilator, and she is having less difficulty with swallowing than at any time in the past. I believe the condition will soon be stabilized. In my opinion too frequent dilatations are contraindicated in this type of case. The local trauma and spasm incident to dilating a tight stricture lead to increased stricture formation caused by persistent inflammation.

Case 2. F. McM., a white man, aged 58, referred by an internist on April 27, 1951, complained of dysphagia following cholecystectomy performed seven weeks previously. Food seemed to lodge in the cervical region of the esophagus. Pain radiated to the back and to the right side of the neck when he attempted to swallow solid food. There was a history of dyspnagia, indigestion and flatulence since boyhood with a tendency for many years to "swell up like a poisoned pup." Since 1947 there had been repeated episodes of pain in the right upper quadrant of the abdomen radiating to the back on the right side. A Roentgen study of the gastrointestinal tract in 1948 yielded no evidence of abnormality except a slight spasm of the duodenum just distal to the cap and several small stones in the gallbladder.

Following an acute episode in March, 1951, cholecystectomy was performed. The gallbladder showed chronic cholecystitis with cholelithiasis; two small calculi were removed. Other than slight vomiting on four occasions, the postoperative course was normal. No feeding tube was

passed. Three weeks postoperatively, the patient could swallow nothing but liquids and complained of inability to swallow properly since the operation. A fusiform narrowing of the lower third of the esophagus for some five inches with the lumen reduced to 4 or 5 mm. in width was demonstrated by barium swallow. Conservative treatment consisted of antacids, liquid and soft diet, and olive oil taken before meals. On gastric analysis before and after administration of histamine, gastric acidity was within normal limits.

Esophagoscopy on April 28, the day after the patient first consulted me, disclosed a whitish membrane approximately 30 cm. from the incisor teeth. It extended along the right lateral wall and could be stripped off easily. The surface was acutely inflamed and bled easily. Distal to this area the esophagus was markedly narrowed and inflamed,

Fig. 5. Case 2.—Roentgenogram showing constant narrowing of the lower portion of the esophagus with dilatation above on March 26, 1952

but there was no evidence of neoplasm. The diagnosis was acute esophagitis. Microscopic examination of the specimen removed for biopsy showed the tissue to be mostly necrotic with no cellular organization remaining. All of the fields were filled with polymorphonuclear leukocytes, degenerated cellular debris and hemorrhage.

The patient improved temporarily on an ulcer diet and antacid therapy, but dysphagia soon became increasingly severe, with substernal burning persisting. On May 5, esophagoscopy was repeated; the inflammatory action was as previously, and there was increased narrowing of the lumen of the esophagus.

At Duke Hospital, Durham, N. C., where the internist then referred the patient, the findings on esophagoscopy were similar, and the diagnosis was nonspecific severe postoperative esophagitis. Following gastrostomy performed there on May 19, he returned to my care for retrograde dilatations, which were begun on July 10 with a No. 34 French Tucker dilator and continued weekly. In August a No. 40 French retrograde dilator was passed with ease. Dilatation with a Hurst dilator was begun in the third week and continued until a No. 30 French dilator could be used with ease. In September, retrograde dilatations were discontinued, and he swallowed a No. 30 French Hurst dilator daily himself. In October, dilatation with a No. 40 French Hurst dilator was carried out with ease, and he used this dilator himself without difficulty.

At esophagoscopy on October 27, the distal portion of the esophagus still appeared narrow and inflamed, with the underlying surface bleeding easily when the whitish exudate was stripped off. There was much less dysphagia, however, with the patient himself using the No. 40 French dilator every 48 to 72 hours without difficulty. The gastrostomy was closed on December 17. Roentgen examination on March 26, 1952, showed the constant narrowing of the lower portion of the esophagus with dilatation above (see Fig. 5).

More than three years have elapsed since the patient first came under my observation, and he now experiences no dysphagia. He carries out dilatation himself with a No. 40 French dilator at monthly intervals or whenever he notices any indication of recurrent dysphagia.

Comment.—The rapid onset of acute reflux esophagitis and stricture formation in this postoperative case in the absence of an indwelling tube or excessive vomiting is of interest. The possibility of esophagitis secondary to the spread of infection by the lymphatic route is suggested. Relaxation of the cardioesophageal orifice at the time of cholecystectomy with bathing of the lower portion of the esophagus with gastric juice is another possibility. In 23.4 per cent of the cases of acute ulcerative esophagitis reported by Butt and Vinson[9] chronic cholecystic disease was present, and in 74.6 per cent the esophagitis occurred following operation. Fifty-two of Bartels' 82 cases were observed following operation.[3]

Reflux Esophagitis Associated with Duodenal Ulcer.—Winkelstein, Wolf, Som, and Marshak[55] reported a series of 20 cases of reflux esophagitis. The patients presented a long history of duodenal or gastric ulcer with a more recent and brief history of esophageal symptoms consisting of dysphagia, heartburn, regurgitation, substernal pain, and loss of weight. Fifteen per cent of them had a duodenal ulcer simultaneously. There were 19 men and one woman in the series. Fourteen were over 60 years of age. These authors suggested that the gastric reflux into the esophagus might result from the hyper-

secretion associated with the duodenal ulcer or from an unexplained decrease in the tone of the cardiac sphincter. Noting the high incidence of their cases in elderly persons, they proposed that a disturbance in the circulatory state of the mucosa or a loss of the mucous barrier might be an etiologic factor. Complications noted by them were esophageal stenosis, hemorrhage and perforation. Stenosis was the most common complication, occurring in nine cases. They suggested that inflammatory swelling, spasm, and fibrous stricture play a part in the formation of the stenosis and that fibrous stenosing esophagitis occurs in the late stages of the severe cases. In a series of 60 cases of benign stricture of the esophagus associated with reflux esophagitis, Benedict and Sweet[6] noted 20 cases in which duodenal ulcer was present.

Wangensteen and Leven,[52] in 1939, performed a gastric resection for massive hemorrhage from a duodenal ulcer on a patient who had a history of esophagitis. She had had frequent esophageal dilatations over a period of four years previously. Following this operation, however, esophageal dilatations were no longer required. Five other patients presenting clinical evidence of esophagitis, esophageal stricture, or both, obtained relief of esophageal obstruction following gastric resection. Believing that esophagitis is probably a manifestation of ulcer disease, these authors suggested that the esophagus doubtless would replace the duodenum as the most common site for ulcers if it received all of the gastric juice as does the duodenum.

Benedict and Gillespie[5] believed that the ulcer diathesis predisposes to the development of esophageal stenosis by virtue of the increased secretion of gastric juice and greater liability of gastric reflux even in the absence of pyloric stenosis. They suggested that the ulcer patient might have changes in the mucosa of the lower portion of the esophagus which make it less resistant to acid peptic action. In 19 of 50 patients with reflux esophagitis with complications subjected to surgery, Sweet, Robbins, Gephart and Wilkins[43] found evidence of ulceration in the duodenum.

Case 3. F. D. C., a white man, aged 59, was referred by an internist on Aug. 29, 1950. He complained of dysphagia, substernal distress, and a sensation of food stoppage under the lower third of the sternum; symp-

toms noticed for several weeks. Several months previously, he related, while eating chicken he had experienced a feeling of obstruction in the upper third of the esophagus, followed by vomiting with no further difficulty in swallowing. There had been two similar episodes in the past several weeks. Roentgen examination on August 21 had demonstrated an area of constant narrowing in the mid portion of the esophagus for a distance of about 4 cm., characterized by smooth margins except for a 1 x 2 mm. projection of barium on the posterior aspect of the esophagus (see Fig. 6). The maximum dilatation in this area was approximately 8 mm. The duodenal cap showed persistent deformity. Interpretation at that time was esophagitis, possibly accompanied by ulceration, and an active chronic duodenal ulcer.

Fig. 6. Case 2.—Roentgenogram showing irregularity of the lower half of the esophagus and active chronic duodenal ulcer on Aug. 21, 1950.

The patient stated that the present illness dated back 20 years. In 1941, a small duodenal ulcer had been diagnosed at Peter Bent Brigham Hospital in Boston. He reported frequent bouts of nausea and vomiting and frequent episodes of epigastric pain, relieved by feedings. Always a high-strung person, he had worked hard and had had long hours. In March, 1950, he had experienced severe attacks of epigastric pain with nausea, vomiting, and hemorrhage from the duodenal ulcer. Nevertheless, despite the Roentgen findings of August 21, when he consulted me a week later, he refused esophagoscopy.

Some two months later he experienced five bouts of severe hemorrhage from the duodenal ulcer. On November 3, Roentgenograms showed a non-

obstructing duodenal ulcer and a small esophageal hiatal hernia apparently accompanied by shortening of the esophagus. The deformity of the duodenal cap was more pronounced than on the previous examination.

The patient consulted me on Jan. 30, 1952, again complaining of inability to swallow. The previous night a piece of meat had obstructed the esophagus completely, and he had been unable to swallow water. Roentgenograms taken just prior to my examination showed narrowing of the lower third of the esophagus with impaction of food. Atropine, given by the Roentgenologist, had relieved the obstruction. Diagnostic esophagoscopy was again refused.

A massive hemorrhage on November 28 necessitated a subtotal gastric resection. A chronic constricting ulcer of the duodenum which showed active bleeding was found.

In June, 1953, the symptoms of substernal burning and food blocking in the midesophagus became worse, especially with emotional stress. In July, I was asked to see the patient again because of complete esophageal obstruction for 48 hours. Esophagoscopy revealed an orange seed obstructing the esophagus 40 cm. from the incisor teeth. Distal to this point the esophagus was greatly narrowed, and at the site of the stricture there was mild inflammatory change in the mucous membrane. The following day it was possible to pass only a No. 18 French Hurst dilator. Dilatations were continued until October 1953, at which time a No. 30 French Hurst dilator was the largest that could be passed. Although he has not returned for further dilatations, the patient recently stated that he still has difficulty occasionally with solid foods, but gets along well if he chews his food thoroughly and eats slowly.

Comment.—The relationship between duodenal ulcer, esophagitis, and esophageal stricture is here illustrated. The association of emotional stress with each bout of esophageal obstruction and the progression of the symptoms following gastric resection are particularly noteworthy. Benedict and Gillespie[5] observed that spasm precipitated by emotional stress superimposed on organic changes accounts for exacerbations in some cases.

Case 4. M. C. D., a white woman, aged 63, first consulted me on July 10, 1953. Her complaints were dysphagia with inability to swallow liquids or saliva except small amounts occasionally and with food seeming to lodge in the midesophagus; pain radiating to the throat, shoulder and hand on the right side; intermittent pain in the epigastrium on the left side, noted especially when she was nervous or upset; frequent unpredictable bouts of substernal burning lasting from four hours to several days; and frequent constipation. There had been no melena.

The patient related that severe vomiting during the last two trimesters of a pregnancy in 1933, with vomiting of blood two or three times daily two weeks prior to delivery, marked the onset of symptoms. Several days after a normal delivery the vomiting ceased. Progressive dysphagia began three weeks later, and within one month she was unable to swallow water. Esophagoscopy was performed in Philadelphia. Correspondence with her physicians there brought the following report: "An esophagoscopy revealed a lesion in the lower third of the esophagus which was treated as a peptic ulcer of the esophagus. She undoubtedly has a short esophagus. She had ulceration in the junction of the esophagus and

stomach. She was treated over a period of five years, having several esophagoscopies and dilatations following which she obtained a great deal of relief."

Thereafter she experienced dysphagia only occasionally until 1948, when she was hospitalized in New Jersey because of recurring episodes of dysphagia and vomiting associated with nervousness and tension. Her physician there stated that she had had previous gallbladder trouble, and that there was evidence suggestive of an ulcer. The Roentgen diagnosis at that time was: "A narrowing of the lowermost 5 centimeters of the esophagus. The upper end of the narrowed area was funnel-shaped and smooth. About 2 centimeters above the cardia, there was a small puddling of barium 3 millimeters in diameter which projected from the

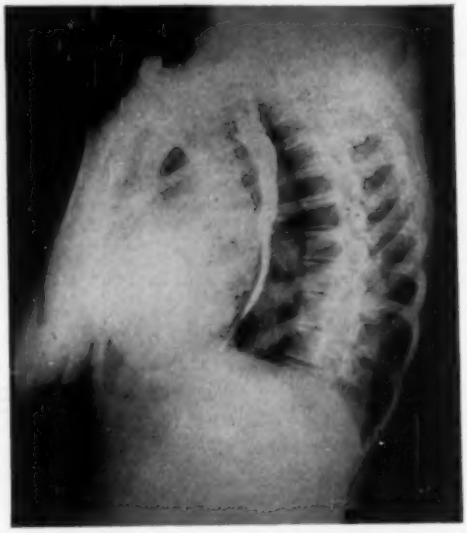

Fig. 7. Case 4.—No Roentgen evidence of esophageal disease reported on July 10, 1953.

right wall of the esophagus. This was interpreted as an ulcer crater until proven otherwise. The duodenal cap was constantly slightly deformed without the demonstration of an active crater. Impression: A narrowed esophagus probably represented scarring from previous inflammation, and the deformed duodenal cap was evidence of an old ulcer history."

Correspondence with her physician in New Jersey stated that esophagoscopic examination at that time revealed stenosis of the distal third of the esophagus with some ulceration of the mucous membrane. Bougies up to No. 24 French were passed with slight difficulty.

The patient then moved to Jacksonville. Recurrent dysphagia led to hospitalization in 1952 under the care of an internist. Roentgenograms

were interpreted as giving evidence of moderate cardiospasm without dilatation, and a deformity of the duodenal cap was attributed to chronic ulcer. It was concluded that there was an active ulcer near the base of the cap. Despite treatment for duodenal ulcer, dysphagia persisted. In June, 1953, she returned to her physician in New Jersey. On esophagoscopic examination, he observed a narrowing of the distal third of the esophagus with ulceration of the mucous membrane. Attempts at passing bougies were unsuccessful. She was unable to swallow a string. His diagnosis was esophagitis with an appreciable degree of cardiospasm and stricture secondary to duodenal ulcer. He referred her to me for further treatment.

A barium swallow on July 10, the day she first consulted me, resulted in negative findings (see Fig. 7), reported as follows: "Examination of the esophagus reveals no evidence of any intrinsic lesion. The esophagus is not dilated, and there is no cardiospasm at this time. The aorta is moderately tortuous and elongated, and the esophagus curls around, but there is no evidence of any obstruction."

On August 13, I performed an esophagoscopy. At a point just above the gastroesophageal junction, there was a narrowing of the esophagus with a horizontal shelf on the right side. Beneath this area there appeared to be a stricture with acutely inflamed mucous membrane. The esophagus was dilated until a No. 21 dilator could be passed with difficulty. The following week a No. 18 French Hurst dilator was the largest I could pass. Subsequent dilatations were carried out over a string at weekly intervals for three months until a No. 27 dilator was employed. The dysphagia then subsided. At present, dilatations are being carried out with a No. 24 Hurst dilator at six to eight week intervals, and she has experienced no further dysphagia. She is now on an ulcer diet and is taking antacids. Except for some heartburn associated with nervousness, she is asymptomatic.

Comment.—In this case there appear to be two contributing causes. The sequence of events probably represents an acute reflux esophagitis following vomiting in pregnancy, progressing through the stages of chronic ulceration, fibrosis, and stricture. Vinson[48] estimated that 10 per cent of benign esophageal strictures result from the vomiting of pregnancy. In all probability the duodenal ulcer is also reactivating the chronic esophagitis from time to time, causing increased stricture formation, esophageal spasm, and symptoms of dysphagia.

The lack of Roentgen evidence of esophageal disease in a patient suffering from severe dysphagia is particularly noteworthy here. Vinson[48] observed that at times the lumen of a stricture is small enough to impede normal swallowing of solid food and yet large enough to permit passage of a thick paste of barium without apparent delay during Roentgenography. If a benign stricture of this type is to be detected, he warned, complete examination of the esophagus is neces-

sary when a patient complains of dysphagia. Several years ago, in a patient under my care, with carcinoma of the esophagus, three esophagrams gave negative evidence, and the diagnosis was finally established by esophagoscopy. Despite normal Roentgenograms, esophagoscopy should be recommended when there is a history of persistent dysphagia.

Association with Hiatal Hernia and Shortened Esophagus.—Two types of hiatal hernia are described by Allison:[2] the paraesophageal and the sliding hernia. A combination of the two may exist.

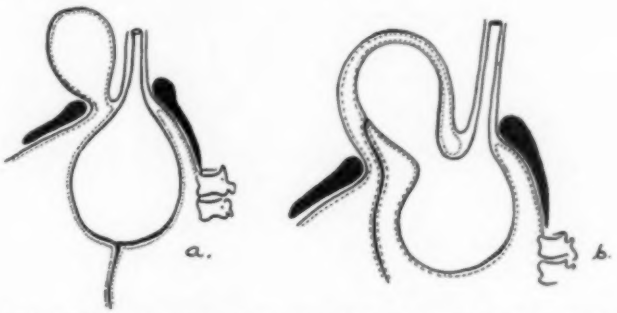

Fig. 8 Preformed peritoneal sac covered by fascia lying in front of the esophagus. b. Anterior wall of the stomach rolled up into the sac to form a paraesophageal hernia. Redrawn from Allison.[2]

A paraesophageal hernia is a herniation of the stomach through a preformed peritoneal sac, which always lies anteriorly to the hiatus. In some persons a protrusion of the peritoneal sac may remain in the hiatus. Allison[2] believed that the hernial sac may remain empty during the patient's entire life, or at any age a part of the anterior surface of the stomach may project into it. If the ligaments of the cardia remain strong, the hernial sac can fill only by the rolling up of the anterior wall of the stomach. In paraesophageal hernias, the esophagus still enters the stomach at an acute angle, and a dilated stomach, when filled, lies between the pericardium and the spine, compressing the esophagus from before backward preventing regurgitation of gastric contents into the esophagus (see Fig. 8). Esophagitis with its symptoms and

sequelae does not develop in patients with this type of hiatal hernia; however, they may complain of fulness after meals and shortness of breath.

In 158 of 170 cases of peptic esophagitis reported by Schmidt[39] esophageal hiatal hernia, either of the short esophagus or of the sliding type, was present. The loss of sphincteric action at the cardia in hernia of these types was highly suggestive of the etiology in this series.

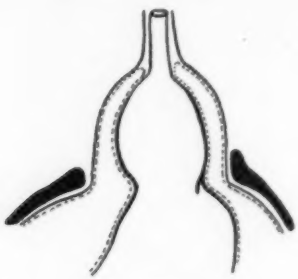

Fig. 9. Diagram of the anatomic relations of sliding hiatal hernia. Note the stretching of the peritoneal reflection and the phrenoesophageal ligament Redrawn from Allison.[2]

The sliding type of hernia occurs when there is a general weakness of the muscles and ligaments at the cardia. The acute angle between the esophagus and the stomach disappears, and the cardia slides up into the mediastinum. In the early phase, the esophagus appears shortened because of its elastic recoil. Allison[2] stated that during this phase the esophagus is not shortened but only relaxed and may be pulled back into its normal position by slight traction of the stomach at operation. The previously described mechanism which normally prevents gastric reflux no longer exists in patients with this type of hernia. In many of them peptic esophagitis develops because of the reflux of gastric contents into the lower portion of the esophagus. In the early stage they may be cured by a simple reduction of the hernia, as advocated by this author (see Fig. 9).

Persistence of the sliding type of hernia leads to the ad-

vanced stages of esophagitis including chronic ulceration and stenosis. The hernia is no longer reducible, and with continued progression of the disease, a resection of the esophagus may become necessary.[2]

Hiatal hernias occur most frequently in the fourth decade of life and later when the tissues about the hiatal orifice are relaxed. An increase in intra-abdominal pressure may be a factor. It has been suggested that hiatal hernia may be caused by an upward traction of the stomach secondary to a shortening of the esophagus in response to some vagal stimulation. Dey, Gilbert, Trump and Roskelley[13] demonstrated a reflex shortening of the esophagus in animals with the production of hiatal hernia due to traction upon the stomach by electrical stimulation of the vagus nerve, or reflexly from stimuli having their origin in the viscera of the upper part of the abdominal cavity.

Esophagitis similar to that occurring in the sliding type of hernia is encountered in patients with a congenitally short esophagus. Some observers believe this to be a rare condition. In many cases, the condition previously diagnosed as congenitally short esophagus probably represents the sequence described by Allison[2] with the shortened esophagus secondary to the loss of the elastic recoil with subsequent maintenance of the retracted position due to scar tissue formation.

Case 5. F. H., a white executive, aged 41, was referred by an internist for esophagoscopy in February 1950. An intense, apprehensive person, he had multiple complaints, most of them apparently functional in nature. Chief among them was pain in the chest of two or three days' duration, associated with a choking sensation. The pain was fairly well localized under the xiphoid process, followed deglutition by a few seconds, was dull in character, brief in duration, and occurred with each act of swallowing. Regurgitation of small amounts of food and gastric juice also was associated with pain.

For 16 years he had had symptoms consisting of substernal discomfort, a sensation of food blocking in the midsternal region and also regurgitation of acid-free food during or shortly after a meal. At intervals of several weeks to several months, episodes of this nature recurred two or three times a week, lasting one to three hours. There was no history of gastrointestinal bleeding or of true vomiting. Cardiospasm frequently had been diagnosed, and on several occasions esophageal dilatation had been advised. Another complaint was cramping in the midepigastrium 15 to 20 minutes after meals, recurring at indefinite periods and with no seasonal relations but always present during periods of strain. Most apprehensive about his throat, the patient was concerned over the possibility of cancer.

General physical and otolaryngologic examinations gave negative re-

sults except for a hyperactive gag reflex. Roentgen examination on February 6 resulted in a diagnosis of esophagitis, hiatal hernia, and possible ulceration of the esophagus (see Fig. 10).

Esophagoscopy on February 11 disclosed an area characterized by inflammatory change 1.5 cm. in diameter on the left posterior lateral wall just above the gastroesophageal hiatus. Approximately 2 cm. above it on the right lateral wall an area of similar size appeared to be inflamed and covered with a whitish exudate. Forty-five centimeters distal to the incisor teeth a wide hiatus opened directly into the stomach. The usual twist of the terminal portion of the esophagus was not noted, and the esophagus appeared to be shortened. The gastric mucosa had a normal appearance.

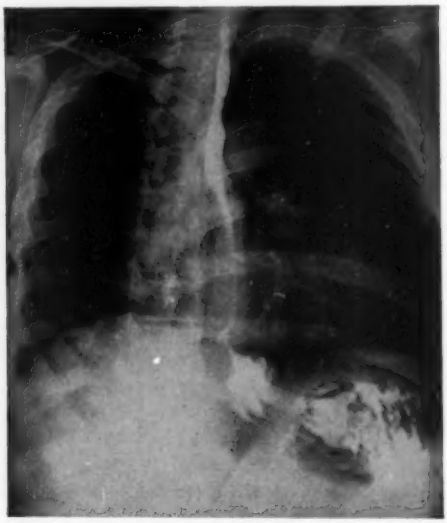

Fig. 10. Case 5.—Roentgenogram showing esophagitis with possible ulceration of the esophagus and hiatal hernia on Feb. 6, 1950.

The patient improved rapidly on an ulcer regimen. On February 17 Roentgen examination again demonstrated a congenitally short esophagus with hiatal hernia and esophagitis. He was discharged from the hospital to continue treatment at home. The final diagnosis was esophagitis, hiatal hernia, short esophagus, and severe anxiety state. He continued to consult me frequently, complaining of fulness in the throat and a choking sensation, and the anxiety about cancer persisted, but no abnormalities were noted in the throat.

On Dec. 6, 1951, the patient was readmitted with an acute attack of severe pain in the chest. Despite recurrence of symptoms for several months similar to those which occasioned hospitalization early in 1950, he had overindulged in barbecued ribs and cabbage the previous day.

His increasing difficulty for some months had more or less paralleled his expenditure of energy in his business affairs. He responded rapidly on an ulcer regimen and rest.

Substernal pain was the chief complaint when he again was hospitalized in June, 1954. Several days previously, a severe burning pain in the lower subxiphoid region had followed by an hour an evening meal of a ham sandwich, coffee and Coca-Cola, preceded by a large meal at noon. The general physical examination once more gave negative results except

Fig. 11. Case 5.—Roentgenogram showing ulceration still present on June 4, 1954.

for a state of anxiety. Roentgen diagnosis was hiatal gastric hernia and possible ulcer crater of the esophagus (see Fig. 11). As previously, an ulcer regimen and rest brought improvement.

Comment.—The symptoms of choking, substernal burning, and food blockage might easily be considered functional in a patient of this type unless the underlying pathologic process is understood. Such symptoms merit careful investigation, including a thorough gastrointestinal examination and diag-

nosis. This case illustrates well the pattern described by Allison[29] and others, which includes the association of hiatal hernia, gastric reflux, esophagitis, esophageal ulcer, and probable shortening of the esophagus, which increases the hiatal hernia and reflux.

Reflux Esophagitis Secondary to Esophageal Surgery.—The dramatic advances in the field of thoracic surgery in recent years have been accompanied by an increased number of operations for cardiospasm and benign stricture of the esophagus. An incompetent cardia too frequently follows this procedure, leading to regurgitation of gastric contents into the lower portion of the esophagus with resultant reflux esophagitis. The time-proved treatment of these conditions with dilatations should not be discarded, and surgical correction should be used only as a last resort. Increasing esophageal resection for malignant disease has increased the incidence of reflux esophagitis for the same reason.

Ripley, Olsen and Kirklin,[36] in evaluating 65 patients who underwent esophagogastrostomy or cardioplasty, found that 28 subsequently had positive signs and 12 had presumptive signs of reflux esophagitis or formation of a stricture. They concluded that the development of techniques to prevent this sequela was needed. Sweet, Robbins, Gephart and Wilkins[43] in 1954 concluded that if a careful choice of operative procedure is made for peptic ulceration and stricture of the lower portion of the esophagus to suit the conditions encountered in the age and physical status of the patient, a satisfactory clinical result may be anticipated in at least 90 per cent of the patients.

Patients subjected to esophageal resection and anastomosis with the stomach and jejunum should be observed closely for symptoms of reflux esophagitis. Prophylactic measures, such as sleeping with the head of the bed elevated and the use of antacids for substernal discomfort, are of value. An esophagoscopy is indicated when definite symptoms are present.

Case 6. N. S. J., a white woman, aged 50, first came under my observation on June 16, 1950. Her chief complaint was difficulty in swallowing for the past three months, solid food seeming to lodge in the region of the xiphoid process. Physical examination gave negative results. Roentgen examination of the esophagus demonstrated an irregularity of the lower

portion. On June 29, I performed an esophagoscopy and noted a raised ulcerated lesion on the posterior and left lateral wall of the esophagus approximately 30 cm. from the incisor teeth. The report on the biopsy was squamous cell carcinoma.

The lower two-thirds of the esophagus was resected on July 1, by the referring surgeon. A high esophagogastrostomy was performed above the arch of the aorta. The patient made an uneventful recovery. She was

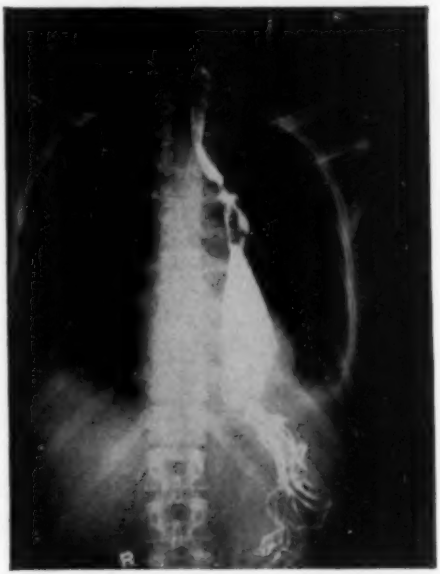

Fig. 12. Case 6.—Roentgenogram showing narrowing of the esophagus at the anastomosis with the stomach on March 14, 1951.

able to swallow a soft diet without difficulty. Four months postoperatively she noted the onset of dysphagia for soft foods. Roentgenograms on March 14, 1951, showed narrowing of the esophagus at the anastomosis with the stomach (see Fig. 12). The next day I performed an esophagoscopy. The esophagus was displaced to the left posteriorly and dilated above the anastomosis. Retained secretions were present. The mucosa was inflamed but intact. The site of the anastomosis was markedly narrowed. A No. 18 French Jackson dilator was introduced through the stricture with difficulty. The dysphagia persisted for three more months. A radical dissection of the glands of the neck on the left side then was performed on October 3 by the referring surgeon for a metastatic carcinoma of the supraclavicular nodes. Again, she made an uneventful recovery.

Recently the patient stated that she is able to eat anything but onions.

She has no complaints except for constipation and occasional pain in the left side of the chest. There is at present no evidence of metastatic disease.

Comment.—This case is presented to show the development of acute reflux esophagitis following esophagogastrostomy.

Case 7. M. B., a Negro woman, aged 48, was referred on May 28, 1954, with the complaint of difficulty in swallowing. The referring surgeon had performed a total gastrectomy, splenectomy, and partial esophagectomy with an esophagojejunostomy on the preceding March 22 for a carcinoma

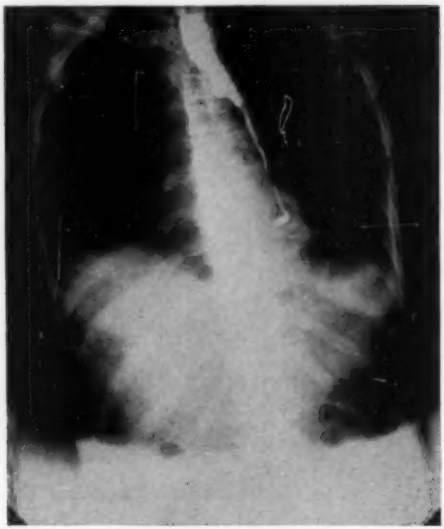

Fig. 13. Case 7.—Roentgenogram showing narrowing of the esophagus at the anastomosis with the jejunum on June 3, 1954.

of the esophagus involving the lower one-third of the esophagus and extending down to the cardia. The lower two-thirds of the esophagus was resected and the anastomosis made above the arch of the aorta. The neoplasm was a squamous cell carcinoma, Grade 4, with extension to the gastric and paraesophageal nodes on the left side. The patient had experienced gradual progressive dysphagia for four months prior to the surgery. A barium swallow revealed almost complete obstruction of the esophagus 6 cm. above the diaphragm. The surgeon noted a poor blood supply of the jejunum manifest by a bluish discoloration at the site of the anastomosis with the esophagus.

For six weeks postoperatively the patient swallowed with little difficulty. Progressive dysphagia then developed, and she complained of epigastric pain. There were intervals of improvement, but the dysphagia

persisted. Roentgenograms on June 3 gave evidence of narrowing of the esophagus at the anastomosis with the jejunum (see Fig. 13). On June 6, I performed an esophagoscopy. The esophagus showed pronounced inflammatory change from just below the cricopharyngeal pinchcock to the site of the anastomosis, where it was markedly narrowed. It was difficult to pass a No. 12 French Jackson dilator through this narrowed area. The mucosa was ulcerated and friable, and bled easily upon manipulation. My diagnosis was acute esophagitis. The course was progressively downhill, and she died of generalized carcinomatosis on June 24. Microscopic section of the esophagus revealed severe esophagitis but no recurrent neoplasm.

Comment.—Severe esophagitis in this instance followed esophagojejunostomy. The poor blood supply of the jejunum may have been an etiologic factor, but it is doubtful that this would account for the esophagitis above the anastomosis. This case would suggest that reflux of intestinal juice is also capable of causing a reflux esophagitis.

TREATMENT.

The majority of patients manifesting symptoms of reflux esophagitis respond to conservative therapy. It is of utmost importance that the symptoms be recognized and the diagnosis established early before the disease has progressed to its later stages. Medical therapy in the early cases consists of antacids, antispasmodics, good oral hygiene, and abstinence from alcohol. The patient should sleep with the head of the bed raised 8 to 12 inches to prevent nocturnal gastric reflux and should continue to do so after the symptoms have subsided.

Since the esophagus is at rest normally except during deglutition, Carver and Sealy[10] advocated three large liquid or semisolid feedings daily in order to decrease esophageal peristaltic activity. They condemned the use of multiple bland diet feedings as used in the treatment of gastric or duodenal ulcers; while such a diet neutralizes gastric juices, it also stimulates gastric motility and the production of more hydrochloric acid and pepsin. Thus, more frequent feedings increase esophageal peristaltic activity. They advocated a glass of water after each meal to clear the lower part of the esophagus of food particles. Also, they prescribed a liquid antacid to be taken at the earliest sign of substernal discomfort and at night before retiring.

Atropine administered 30 minutes before meals will reduce

spasm and gastric secretions. Antibiotics may be used parenterally or orally for secondary infection. Rogers[37] prescribed 0.5 Gm. of streptomycin in 5 cc. of saline solution to be taken two to four times daily. Gentle bouginage may be carried out for spasm or early stenosis. Carver and Sealy[10] advocated continuing treatment until the patient is free of pain for at least two weeks, three consecutive stools show no occult blood, and Roentgenograms show no evidence of an ulcer crater or delay of barium passage through the lower third of the esophagus. A bland diet should be taken for two or three months after symptoms have subsided.

Allison[2] favored a repair of the diaphragm in patients with a sliding hiatal hernia before a permanent esophageal shortening has occurred. This restores the normal cardioesophageal mechanism and prevents the progressive phases of reflux esophagitis.

Chronic ulceration and stricture are manifest by the symptoms of dysphagia. In addition to conservative management, a program of bouginage must be instituted. This is best carried out by dilatation over a string. When sufficient dilatation is obtained by dilating over the string, Hurst mercury-filled bougies may then be employed. The patient may be taught to dilate the esophagus himself with these. Dilatations are begun at weekly intervals, and the interval is increased as soon as possible. Too frequent dilatations may prevent healing and increase spasm. In severe cases temporary gastrostomy and retrograde dilatations may be necessary. Gastrostomy is advantageous in maintaining an adequate nutrition and placing the esophagus at rest.[10]

Sweet, Robbins, Gephart and Wilkins[43] advocated surgical measures in any case of ulcer or stricture of the esophagus in which there is a history of bleeding, obstruction unsuccessfully treated by bouginage, intractable pain, or in some instances evidence of perforation. They concluded that if a careful choice of operative procedure is made to meet the conditions encountered and the age and physical status of the patient, a satisfactory clinical result can be anticipated in at least 90 per cent of the patients. Operative procedures advocated by them were a limited esophageal resection with end

to end anastomosis, esophagoplasty, and partial esophagectomy and gastrectomy with an esophagogastro-anastomosis. Carver and Sealy[10] preferred subtotal gastric resection with repair of hiatal hernia for the treatment of patients with a triad of esophageal ulcer, hiatal hernia and duodenal ulcer. Wangensteen and Leven[52] believed that the merit of gastrectomy as a therapeutic agent for the relief of esophageal obstruction secondary to ulcer disease is that it reduces the acidity and digestive capacity of the gastric juice and quickens the gastric emptying time.

Benedict and Gillespie[5] stated that gastric resection for esophageal stenosis and the presence of duodenal ulcer is theoretically justified so far as it reduces the volume of gastric secretion, but there is inadequate evidence of its prophylactic or curative value at present. They concluded that it is desirable to repair hiatal hernias that are causing symptoms and do not respond to other measures, but believe there is inadequate evidence at present to prove the value of repair operations as a prophylactic measure.

COMMENT.

Recognition of the early symptoms of reflux esophagitis is important if the progress of the disease is to be prevented. Familiarity with the closing mechanism of the esophagocardiac junction is essential to the understanding of this disease. Impaired function of this mechanism allows a reflux of gastric contents with a high acid pepsin concentration to have a corrosive effect on the esophageal mucosa. The devastating effect of the action on the nonresistant squamous mucosa of the lower portion of the esophagus has been demonstrated experimentally. This process causes an acute erosive esophagitis to develop, which progresses in the absence of medical management to an acute ulcerative esophagitis with subsequent destruction of the muscularis coat, which finally terminates in a cicatricial stenosis of the esophagus. Hemorrhage and perforation may occur as complications. The symptoms of reflux esophagitis associated with sliding hiatal hernia, duodenal and gastric ulcer, congenitally short esophagus, and vomiting, and those occurring postoperatively deserve careful investigation on the part of the physician if this disease

process is to be arrested. One should be most hesitant before labeling such complaints as functional.

Diagnostic procedure should be advocated early and medical management instituted as soon as the diagnosis is established. The majority of the patients with reflux esophagitis respond to medical management. Repair of sliding hiatal hernia is advocated if medical management fails in cases of this type.[2] Surgical intervention is advised in cases of ulcer or stricture of the esophagus when there is a history of bleeding, obstruction unsuccessfully treated by bouginage, intractable pain, or evidence of perforation.[43] In spite of normal Roentgen findings, diagnostic esophagoscopy should be performed when unexplained symptoms pertaining to the upper part of the gastrointestinal tract persist.

SUMMARY.

The anatomy and physiology of the esophagus, particularly of the lower portion, are described.

The etiology of esophagitis due to reflux of gastric contents into the lower portion of the esophagus is discussed. Seven cases are presented and commented on to illustrate various causes of reflux esophagitis.

The pathologic changes, symptoms, diagnosis and medical and surgical management of this disease are presented briefly.

Esophagoscopy is of the utmost importance in the final diagnosis and understanding of this disease.

It is essential that the otolaryngologist be well aware of the symptoms, the characteristic pathologic changes, and the sequelae of reflux esophagitis.

Likewise, the internist, the surgeon and the general practitioner all may benefit by familiarity with the various aspects of this disease so that early recognition and remedial measures may combat both the disease and a tendency among physicians to regard its initial manifestations as functional in nature.

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TRACHEOBRONCHIAL INVOLVEMENT SECONDARY TO PULMONARY TUBERCULOSIS.

The Role of the Bronchoscopist in Its Management.*

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FOREWORD.

This thesis has for its purpose an analysis of the role of the bronchoscopist in pulmonary tuberculosis, with particular reference to involvement of the tracheobronchial tree, and also with particular reference to his function in a tuberculosis section attached to a large general hospital.

This purpose has been accomplished in two ways:

1. By a review of 200 recent bronchoscopies performed on tuberculosis subjects in a hospital of this kind.

2. By a review of the literature, including a review of the more important of the early publications on bronchoscopic diagnosis of tracheobronchial involvement in pulmonary tuberculosis. Special features of the 200 cases analyzed are discussed in the light of this review.

HISTORICAL NOTE.

In an interesting and excellent review of the development of the concept of tracheobronchial tuberculosis as a complication of pulmonary tuberculosis, Smart[1] pointed out that the earliest mention of tuberculous lesions in the tracheobronchial tree was by Richard Morton in 1694, the same Morton, incidentally, who originated the word phthisiology. The condition was so well described by Cayol in 1810 that his thesis on the subject was referred to in complimentary terms by Laennec in 1829, in *Mediate Auscultation and Diseases of the Chest.*

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Although Laennec thought the complication unusual, he devoted several pages to bronchial ulceration; stenosis, wheeze and rhonchi were described as characteristic.

Meantime Louis, in 1825, had given an excellent description of the appearance of bronchi in the neighborhood of tuberculous cavities and had also described tuberculosis of the larynx, the epiglottis and the trachea. There were only seven cases of tracheobronchial tuberculosis in the 102 cases of pulmonary tuberculosis on which his remarks were based, but the incidence of bronchial involvement would probably have been greater, as he stated, if his examination of these structures had been more detailed.

In spite of the excellence of these early descriptions, clinicians were not greatly impressed by possible involvement of the tracheobronchial tree in pulmonary tuberculosis. Stokes in 1837, in *Diseases of the Chest*, stated that he would not occupy many pages with this subject because it was "of more interest to the pathological anatomist than to the student of diagnosis." More than a hundred years later, in 1938, Warren, Hammond and Tuttle[2] observed that there was no better example in clinical medicine of slowness to grasp the observations of the pathologist and turn them to use than tracheobronchitis, which had for so many years remained "a textbook legend."

To continue with Smart's account, Rokitansky in his textbook of pathology published in 1842 gave a good description of the relation of endobronchial ulceration to cavitation. Heinze, in 1879, found an 8 per cent incidence of tracheal involvement in 1,226 cases of pulmonary tuberculosis. He did not investigate the bronchi. Eppinger the following year described the type of miliary laryngeal and tracheal tuberculosis which exists without pulmonary cavitation. All of these descriptions, as several observers have noted, antedated the discovery of the tubercle bacillus by Koch in 1882.

After this period, as Smart puts it, tracheobronchial tuberculosis "passed into considerable neglect." It was mentioned only occasionally during the next 40 years, and it seems to have received no clinical consideration at all.

Interest in it was revived in 1924, when Heaf[3] published a study of tuberculous lesions in the trachea; they were found in 44 per cent of 133 autopsies performed in tuberculosis subjects at the Colindale Hospital in Hendon. He gave an excellent clinical description of tracheal involvement but did not mention bronchial lesions. In 1929 Minkovsky,[4] in an analysis of 2,584 autopsies on tuberculous subjects at a hospital in Leningrad, reported that the larynx was involved in 19 per cent of all cases and the trachea in 11.4 per cent. Like Heaf, he made no mention of bronchial involvement.

Interest in tuberculous lesions of the bronchial tree in pulmonary tuberculosis was a development of the next few years. At first it was limited almost exclusively to the United States. It was not until 1939, as Smart points out, that the first paper on the subject, by Morlock and Hudson, appeared in the British medical literature. Young,[5] in 1953, doubted that tracheobronchial tuberculosis had been of great importance in Great Britain 30 years earlier and suggested that the current incidence might indicate a change in the pattern of the disease. Smart's reasoning seems more logical. When bronchoscopies began to be performed in considerable numbers in Great Britain, he said, the disease promptly became as common there as it was in the United States.

An interesting comment on the comparative incidence of tracheobronchial disease in the two countries was made by Jarman[6] in 1949. Although he was then practicing in Wales, his experience with the disease had been obtained at a sanatorium in Michigan. Lesions of the major bronchi were diagnosed so much more often in the United States than in Great Britain, he said, that the question had arisen whether they were being over-diagnosed in the former country and under-diagnosed in the latter. Without committing himself as to possible under-diagnosis in the United Kingdom, he stated that his personal American experience had convinced him that they were not being over-diagnosed in the United States, in which because of racial and geographic factors, they might perhaps be really commoner.

The classic reports of Eloesser, Samson and their associates on tracheobronchitis are still worth reading. Their concepts,

however, were slow to spread. In 1934 Eloesser[7] wrote that stenosis of the larger air passages was "the stepchild of clinical medicine." In 1937 Samson[8] complained that the literature to date had chiefly been devoted to the obstructive variety of tracheobronchitis and that the clinical recognition of the earlier, non-obstructive manifestations of the disease was still being seriously neglected. It is a tacit commentary on the general unfamiliarity with the condition that a year earlier the *American Review of Tuberculosis* had provided space for the publication of 18 detailed case histories of tracheobronchial tuberculosis.[9]

The continued ignorance of the disease might have been expected. Most of the early reports were derived from post-mortem material and contained little of interest, it was thought, for the clinician; furthermore, tracheobronchial tuberculosis can be diagnosed positively only by the bronchoscope, and bronchoscopy in pulmonary tuberculosis had not yet been generally accepted. Half a dozen recent writers have commented on the fact that as late as 1927 Chevalier Jackson, the father of bronchoscopy in this country, stated that it was of no great use in tuberculosis. Myerson[10] in 1936 remarked that the "most authoritative work on bronchoscopy" (presumably Jackson's text) gave only a page to the use of the bronchoscope in tuberculosis. One writer stated that some observers "even advocate it" in the absence of any suspicion of tracheobronchial disease, merely because thoracoplasty was to be performed. One gathers from what was left unsaid, rather than from what was said, just how daring that policy was.

By 1944, however, the situation had begun to change. In that year a symposium on tracheobronchitis was held at the annual Congress of the American College of Chest Physicians, and the January-February, 1945, issue of *Diseases of the Chest* was given over entirely to the publication of the proceedings.[11] Stone, in the introduction to this special issue, wrote "Is it too much to hope that the future chest specialist will not only be expert with his stethoscope, X-ray interpretations and clinical evaluation, but that he will also be adept with the bronchoscope?"

At this symposium Overholt and Wilson[12] presented what they called a preliminary report on pulmonary resection in tuberculosis complicated by tuberculous bronchitis. The two significant developments in pulmonary tuberculosis in the past decade, they said, were *1*, the knowledge that had been gained concerning tuberculous tracheobronchitis, and *2*, the accomplishment of lobectomy and pneumonectomy in tuberculosis with such a margin of safety that resectional surgery had now to be considered in all therapeutic programs. They might have gone further and said that underlying the increased knowledge of tracheobronchial tuberculosis was the increased use of bronchoscopy, which had made its recognition possible.

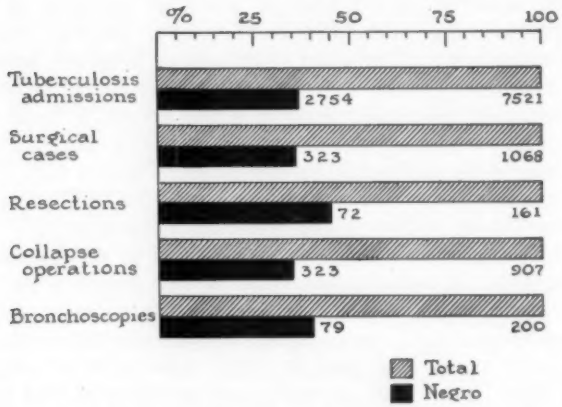

Fig. 1. Tuberculosis at Charity Hospital, 1946-1953, with special reference to the negro; general data.

MATERIALS AND BACKGROUND.

The 200 bronchoscopies which form the basis of this thesis were performed on tuberculous subjects at Charity Hospital of Louisiana in New Orleans, between 1946 and 1953 inclusive. This hospital does not operate a sanatorium in any sense of the word, but as a matter of necessity it has always had a large tuberculous population. The policy of admission, which is adhered to as strictly as possible, is to accept only patients

with active disease, who conceivably would respond to therapy.

The large negro population (see Fig. 1) presents innumerable special problems peculiar to this hospital and this part of the country. These problems are particularly urgent in tuberculosis, a disease of high incidence in this race. Although the negro admissions to the hospital now far outnumber the white, the physical facilities for negro tuberculous subjects are somewhat less than for the white (see Fig. 1), and the turnover of beds is smaller because, in the opinion of those in charge of the tuberculosis units, the negroes, case for case, present more serious disease than white subjects.

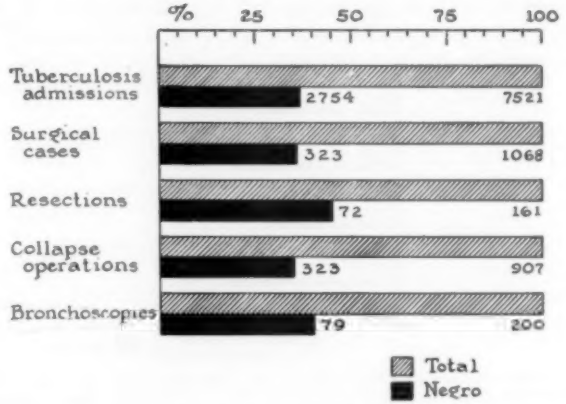

Fig. 2. Tuberculosis at Charity Hospital, 1946-1953, with special reference to the negro; surgery.

The proportion of surgery performed in the negro unit (see Fig. 2) is practically the same as the proportion of negro admissions to the hospital for tuberculosis, but the proportion of resections is higher, which is in line, it would seem, with the greater seriousness of the disease in this race. Both the general hospital mortality for tuberculosis and the surgical mortality are also proportionately larger in the negro race (see Fig. 3).

As these figures indicate, pulmonary tuberculosis is still providing a large number of hospital admissions. It is still

attended with a high hospital death rate, and the hospital deaths, of course, represent only a small proportion of the total death rate. This is particularly true of negroes, for whom hospital facilities for tuberculosis are totally inadequate in this special area. The local situation reflects the national situation. According to Bureau of Census Reports,[13] there were 34,102 deaths from pulmonary tuberculosis (unqualified) in 1949, 29,228 in 1950, and 26,644 in 1951. That the concept of tracheobronchial involvement in pulmonary tuberculosis is still not general is shown by the fact that during these three years only 35 deaths were listed as due to "tracheobronchial glandular tuberculosis with symptoms."

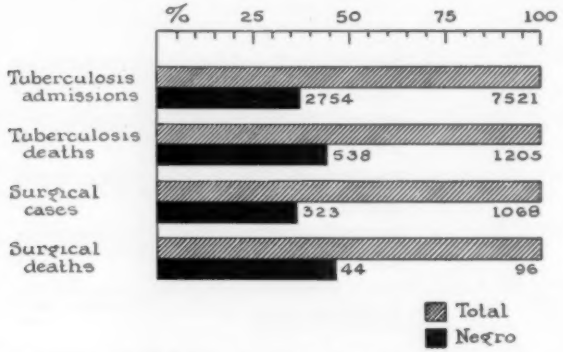

Fig. 3. Tuberculosis at Charity Hospital, 1946-1953, with special reference to the negro; mortalities.

INCIDENCE.

Eloesser[7] said in 1934 that stenosis of the major bronchi was so frequent in pulmonary tuberculosis that it was difficult to understand how the condition had escaped attention for so long. At that time there was certainly no understanding of the true incidence of tracheobronchial involvement in pulmonary tuberculosis. Epstein and Ornstein,[14] in 1936, pointed out that Myerson, in 1929, had said that bronchial involvement in tuberculosis was probably not infrequent, but involvement of bronchi accessible to endoscopic study was in his opinion very infrequent. They also cite Clerf's statement in 1931, that

involvement of the mucosa of the larger bronchi was apparently rare. In 1935 Graham[15] stated that he had never found involvement of the major bronchi in any of the cases he had bronchoscoped, and slightly less space is devoted to tracheobronchial tuberculosis in his text on surgical diseases of the chest than to syphilis of the tracheobronchial tree.

Even in 1954 the true incidence of involvement of the trachea and bronchi in pulmonary tuberculosis is still far from clear. One thing, however, is very clear: although the importance of this complication is now generally accepted, its frequency is still greatly underestimated. The reason is a sort of vicious circle, because the frequency of the complication is underestimated, bronchoscopy is not employed as often as it should be. Because bronchoscopy is employed less often than it should be, the frequency of the disease is not appreciated.

One reason why the reported frequency varies so widely is that the reported series are made up on widely different bases (see Table 1). All stages of the primary disease are represented in them. Some reports include laryngeal as well as tracheobronchial involvement. Some are based on routine admissions, others on cases referred for bronchoscopy because of suspicion of the disease. Still other reports are based on postmortem studies, which were probably not always conducted by the same techniques.

Flance and Wheeler,[17] who reported the lowest autopsy incidence, stated that they had studied the tracheobronchial tree, down to the third order of bronchi, with special care. Daly and his associates,[24] whose study covers only children, consider that diagnostic acumen plays a part in the reported frequency. Thirty of the last 90 children whom they bronchoscoped were found to have endobronchial disease, and they regard this proportion (33.3 per cent) as probably more representative than the 10 per cent incidence in their total series of 434 patients.

The best of the recent reports, and in many respects one of the best ever made, is by Houghton and Joules,[26] on clinical material collected under the auspices of the British Tubercu-

TABLE 1 — INCIDENCE OF TRACHEOBRONCHIAL TUBERCULOSIS IN VARIOUS REPORTED SERIES.

Year	Authors	Source of Material	Cases Studied	Tracheobronchial Disease	Percentage
1939	McIndoe et al.[16]	Majority admissions	272	30 positive 13 questionable	11.0
1939	Flance and Wheeler[17]	Autopsies	285	9	3.2
1939	Hawkins[18]	Selective*	516	132	25.6
1938	Myerson[19]	Selective	100	31	31
1940	Myerson[20]	Selective	236	52	22.0
1942	Wilber**[21]	Autopsies	500	177	35.4
1945	Acuna[22]	Selective	279	83	29.7
1945	Silverman[23]	Autopsies	110	66	60.0
1949	Jarman[6]	Selective	800	206	25.7
1952	Daly et al.[24]	Selective***	434	43	10.0
1953	Olson et al.[25]	Resected specimens	602	122	20.3
1954	Houghton and Joules[26]	Admissions****	386	131	33.9
		Resected specimens	95	39*****	41.0
1954	Candidate	Selective	200	66	33.0

* Bronchoscopies, performed on referred patients.

** This material apparently overlaps Myerson's material from the same institution (Sea View).

*** Children only.

**** Every fifth admission in six cooperating hospitals.

***** 39 cases were positive bronchoscopically. When the specimens were examined histologically, the number of cases with tracheobronchial involvement rose to 90.

losis Association. Eight hospitals cooperated, including two in which the study was limited to surgical cases. In the other hospitals, every fifth patient admitted was selected for bronchoscopy, regardless of the status of the disease or any other consideration. As far as possible, the bronchoscopies performed in each hospital were performed by the same operators. All reports were made on the same uniform simplified basis, and the laboratory studies of surgical specimens were conducted according to uniform techniques.

In the 386 cases thus studied at six English hospitals, tracheobronchial disease was diagnosed in 131 — 33.9 per cent. This is probably a fair average. It almost precisely parallels the 33.3 per cent incidence reported in this thesis from the Charity Hospital in New Orleans, La. The wide range of positive cases at the various English hospitals is more conveniently discussed under the heading of clinical diagnosis. For the same reason the histologic studies in the Houghton and Joules report are also discussed under another heading.

INCIDENCE IN RELATION TO RACE, SEX AND AGE.

The negro incidence of tracheobronchial disease in this series (see Fig. 4) was higher than the white — 39 per cent to 28.9 per cent. This series is small, but the higher negro incidence is significant to those who are familiar with the special problems of pulmonary tuberculosis in this race. The same comment holds for the sex incidence in the two races (see Fig. 4). In the 43 negro women who were bronchoscoped the percentage of tracheobronchial disease was 41.6.

What little the literature contains on the subject of tracheobronchial disease in negroes generally bears out the observations at this institution, though no other hospital has so large a proportion of negroes in its population. Wilber,[21] who pointed out that her observations were the first on the subject, found tracheobronchial disease at Sea View Hospital in 95 of 180 postmortem examinations in negroes against 111 of 291 examinations in white subjects. The hospital admissions for the period covered by the autopsy study were preponderantly white (3,784 against 1,678).

Daly and his associates,[24] in their studies on children at Bellevue Hospital, found tracheobronchial disease in 18 of 144 negroes, against 19 of 165 Puerto Ricans, and 6 of 121 white children. Himelstein,[27] who cites no figures, states that tracheobronchial disease is more common in negroes, aborigines and teen-agers because of the higher incidence of exudative disease in these groups.

The internists at the Charity Hospital report a high incidence of exudative disease in their negro patients. Silverman,[23] at the Triboro Hospital, found no correlations in age, sex or race in 66 cases of tracheobronchial disease diagnosed at postmortem, but there were only 13 negroes in the 110 autopsied cases from which these conclusions were drawn.

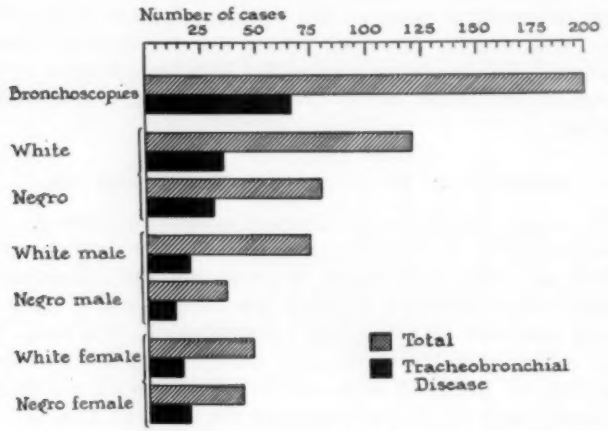

Fig. 4. Incidence of tracheobronchial involvement according to race and sex in 200 bronchoscopies on tuberculous subjects, Charity Hospital, 1946-1953.

Most reports show, as does this series, a higher incidence of tracheobronchial disease in females, though no special observations seem to have been made on negro females. Some observers attribute it to the breakdown of tuberculous tissue which is frequent during pregnancy. Himelstein[27] explains it by the smaller caliber of the female bronchus, and recalls Jackson's observations that encroachment on the lumen of

the female bronchus, even though it is of small magnitude, can produce distal disturbances out of all proportion to the degree of narrowing.

Endobronchial disease can occur at any age, the wide spread observed at the Charity Hospital (see Fig. 5) being apparent in all reported series. In Wilber's[21] studies from Sea View Hospital, for instance, the age range in 177 cases of tracheobronchial disease was from one to 79 years. The highest incidence was in the third decade, in which the largest number of autopsies were performed.

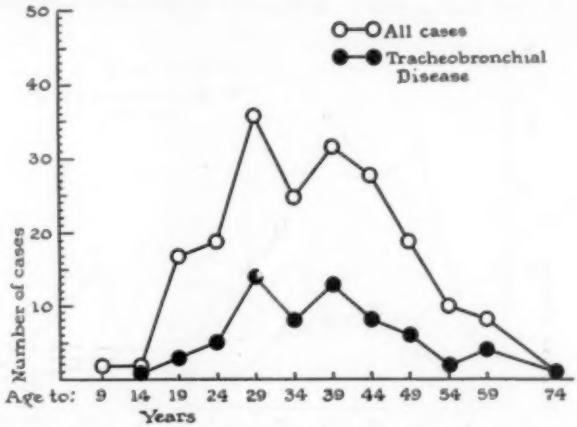

Fig. 5. Incidence of tracheobronchial involvement according to age in 200 bronchoscopies on tuberculous subjects, Charity Hospital, 1946-1953.

In the study on children by Daly and his associates[24] at Bellevue Hospital, the age range was from four months to nine years; 48.4 per cent of the 434 children in the whole series were under three years of age, but 69.8 per cent of the bronchial involvement was in this group. No special observations seem to have been reported on age in negro subjects.

INCIDENCE IN RELATION TO DURATION OF SYMPTOMS.

The duration of the disease is sometimes stated to be a factor in the incidence of tracheobronchial disease. An analysis of the bronchoscopies performed for pulmonary tubercu-

losis at the Charity Hospital does not support this point of view (see Fig. 6). Tracheobronchial involvement appeared in patients who had symptoms of the disease less than a month, as well as in those who had it for 18 years.

The chief significance of these observations is that tracheobronchial involvement is not infrequent and must not be overlooked in early cases of pulmonary tuberculosis. They are borne out by other reports. Overholt and Wilson,[12] for instance, found the duration in 30 cases in which resection was performed, to be from seven weeks to 18 years; nine patients had been ill less than a year. Meissner,[28] apparently including the

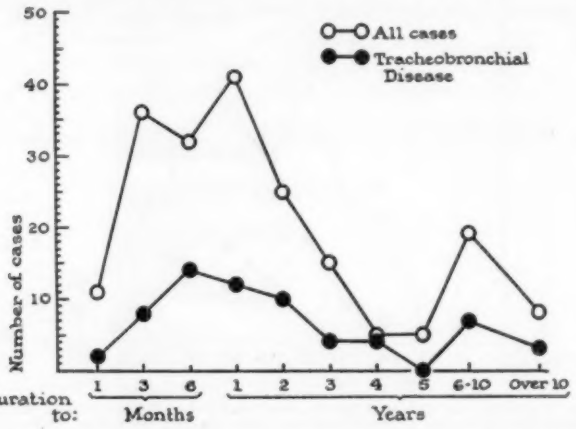

Fig. 6. Incidence of tracheobronchial involvement according to duration of symptoms in 197 bronchoscopies on tuberculous subjects, Charity Hospital, 1946-1953.

same material in a larger series (60 cases), also found the duration in a third of the cases to be less than a year.

INCIDENCE ACCORDING TO LOCATION OF LESION.

The location of the lesions of tracheobronchial involvement in the 66 bronchoscopically positive cases (see Fig. 7) cannot be correlated with the location of the parenchymal disease, which was as follows: Diffuse involvement of the right lung, 51 cases, and of the left lung, 56 cases; right upper lobe, 95

cases, left upper lobe, 37 cases; right middle lobe, 3 cases; right lower lobe, 6 cases, left lower lobe, 4 cases. Parenchymal disease was present in the right lung in 153 cases and in the left lung in 97. In the 66 cases of endobronchial disease, the involvement was on the right side in 44 cases and on the left in 33. These figures, all of which are overlapping, include the 47 bilateral parenchymal lesions and the 11 bilateral tracheobronchial lesions.

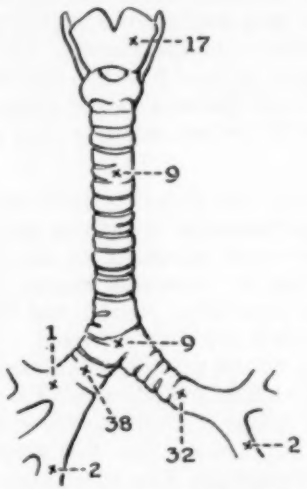

Fig. 7. Anatomic distribution of tracheobronchial involvement of 66 bronchoscoped tuberculous subjects, Charity Hospital, 1946-1953.

In this series, as in most reported series, it was generally true that unilateral endobronchial involvement was almost always present on the same side as the parenchymal lesion or, if the involvement was bilateral, the endobronchial lesion was more advanced on the side of the unilateral parenchymal lesion. Bilateral endobronchial disease was not necessarily associated with bilateral parenchymal disease, and vice versa. These cases also demonstrated, as Myerson[20] has pointed out, that relatively few bronchoscopic examinations are done early enough to be certain of the particular branch bronchus from which the infectious process spread.

PATHOGENESIS.

There are two theories as to how tracheobronchial involvement develops in pulmonary tuberculosis:

1. Reichle and Frost[29] in 1934 advanced the theory that infection probably spreads to the bronchi and trachea by way of the lymphatic system. By this theory, to express it as simply as possible, the lymphatic structures surrounding the major bronchi and the trachea absorb infected material from the periphery of the lung and carry it through the walls of the bronchi, and thence into the mucosa. This is of course a perfectly reasonable mode of infection, but Meissner[28] believes that if it occurs, the tracheobronchial disease will present as gross lesions only at certain selective sites along the path of progression.

2. Bugher, Littig and Culp,[30] in 1937, while granting that invasion from peribronchial structures may occur by direct extension in some cases, advanced the counter theory that in most cases infection is by surface implantation. This seems the most obvious possibility. Reichle and Frost,[29] while they do not eliminate this mode of infection, consider that it is usually prevented by the protective influences of cilia, mucus and bronchial peristalsis. In their opinion, if surface implantation occurs at all it is only after massive eruptions of caseous material. They also believe that this form of infection is chiefly limited to secondary bronchi of a lower lobe, which is the seat of bronchogenic distribution from a large apical cavity.

The general experience does not support Reichle and Frost's views. Most observers believe that implantation infection is the overwhelming mode of extension. They also believe that it may occur in any part of the respiratory tract, and is not limited to the lower lobe. The site of predilection, for mechanical reasons, is the posterior or posterolateral wall of whatever bronchus may be involved.

Infection by contiguity is an obvious possibility whenever a cavity in the lung is adjacent to a major bronchus. Few observers, although the possibility naturally exists, consider hematogenous spread of any real significance. There also

seems little ground for the assumption that tracheal lesions are secondary to laryngeal lesions. Both, instead, probably take their origin from the original pulmonary parenchymal disease.

BRONCHOSCOPIC OBSERVATIONS.

Samson,[8] one of the earliest workers in the field of tracheobronchial involvement in pulmonary tuberculosis, listed four types of lesions observed bronchoscopically and noted that they might exist in combination. Bronchoscopic studies at the

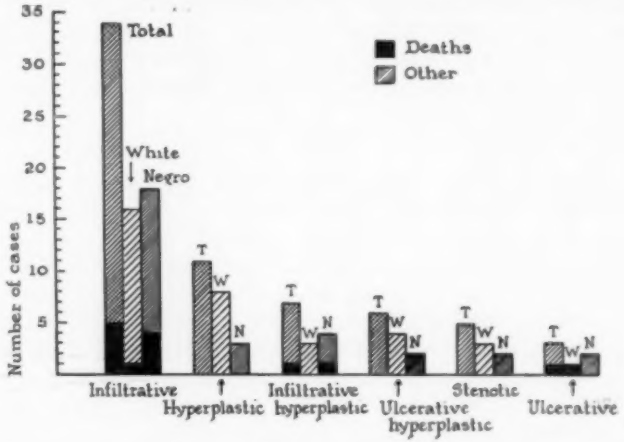

Fig. 8. Distribution of pathologic processes in 66 bronchoscopically diagnosed cases of tuberculous tracheobronchitis, Charity Hospital, 1946-1953.

Charity Hospital indicate that his classification is still valid and sound (see Fig. 8). It is as follows:

1. The nonulcerative, nonstenotic type of lesion is an infiltrative process in the submucosa, characterized by the presence of occasional discrete tubercles. The overlying mucosa, while not grossly ulcerated, is congested, granular and edematous and bleeds easily.

2. In the hyperplastic type of lesion the pathologic changes are similar to those just described but are greater in degree. The submucosal process is proliferative, and conglomerate

tubercles or tuberculomas are often demonstrable. In this type of lesion there is beginning encroachment on the lumen, sometimes of considerable extent.

3. The ulcerative type of lesion is characterized by grossly visible circumscribed or diffuse loss of mucosa. Pyogenic infections are frequently superimposed.

4. In the fibrostenotic type of lesion, stenosis may be localized or diffuse. While the preceding process may have been proliferative or even infiltrative, it has most often been an ulcerative process which has healed with the formation of fibrous tissue. Stenotic lesions were surprisingly few in this material, but in one of the cases it was possible to determine that the antecedent disease had been infiltrative, hyperplastic and ulcerative.

The comments of some observers on the pathologic process as it is determined bronchoscopically might be mentioned. Himelstein[27] points out that if, as Meissner says, the earliest lesion is a submucosal tubercle, it is logical that the earliest visible manifestation would be an infiltrative edema, which might present as an obliteration of the normal depressions between the cartilaginous rings. Himelstein also observes that it is not usual to find ulceration taking the form of the ordinary punched-out, circumscribed lesion. When such a lesion is present it indicates, in his opinion, an overwhelming infection by surface implantation.

Overholt and Wilson,[12] basing their remarks on a study of 30 resected specimens, stated that the predominant pathologic process is submucosal involvement with round-cell infiltration, usually accompanied by tubercle-formation. Wilber[21] considered ulceration the definitive lesion; it was present in his series in 177 of 248 autopsied cases. In children, according to Daly and his associates,[24] the first pattern of disease may be bronchial compression without mucosal involvement. Edema and inflammation may precede ulceration and granulation. Erosion of the bronchial wall by infected lymph nodes is a possibility in children, as might be expected, but is uncommon in adults, also as might be expected.

Wilson[31] emphasizes that the first evidence of a stenotic

lesion is likely to be stagnation of secretions. Even when there is no demonstrable stenosis, loss of ciliary action and decreased bronchial peristalsis result in their clinging to the bronchial wall, where they may be mistaken for tubercles. A practical method of determining the nature of these patches is by the use of suction; secretions will disappear while tubercles will remain.

Interpretation of Bronchoscopic Observation. The cardinal consideration for the bronchoscopist to bear in mind in studying pulmonary tuberculosis, as well as all other diseases, is that gross appearances are often deceptive, and that an apparently normal bronchus may actually be the site of an extensive disease process. In other words, useful as this technique is, it has definite limitations.

The first of these limitations is that the bronchoscopist is limited by the physical range of his vision. He cannot see more, in the order of their visualization, than the following structures:

1. The larynx.
2. The trachea.
3. The carina and bifurcation.
4. On the right, the main bronchus; the orifice of the right upper lobe bronchus; the orifice of the middle lobe bronchus; the five segmental orifices of the lower lobe.
5. On the left, the main bronchus; the orifice of the left upper lobe bronchus; the four segmental orifices of the lower lobe.

Within these visual limitations, the bronchoscopist can see changes in the mucosa, dilatation of the lumen, and distortion and other alterations in the lumen. Clearly obstructing lesions, which are the cause of stenosis and subsequent atelectasis, are easily visualized. Minor stenotic lesions are difficult or impossible to visualize, though their presence can often be inferred. Lesions in the upper lobe bronchi usually cannot be visualized. The temptation to demonstrate suspected lesions "around the corner" with opaque oil should be resisted. This method supplies a great deal of information but only at

the cost of masking the future course of the disease by the continued presence of the opaque solution.

The bronchoscopist's function goes considerably beyond merely reporting what he can see through his instrument. He must decide what is normal and what is not. This is no easy matter. It is not at all safe to assume that absence of visible changes is equivalent to negative findings. Clear proof to the contrary will be adduced shortly. There is no doubt, however, that when even minor gross changes are observed, tracheobronchial disease is present. It is also axiomatic that the more pronounced the structural changes, the more severe the disease process is likely to be.

What eventually happens to every bronchoscopist is that as his experience increases, he sets up his own criteria of normal and abnormal findings. Jackson and Jackson,[32] for instance, stress the importance of color changes; but a reddened mucosa, as Houghton and Joules[26] point out, may be caused by coughing induced by instrumentation, as well as by pathologic changes.

If the altered coloration is due to trauma, it will disappear promptly if manipulations are discontinued for a few minutes. Congestion caused by coughing is more likely to be persistent. In at least one case in this series, which was finally classified as normal, the bronchoscopist noted that the unusual degree of congestion had almost led him to report tracheobronchial disease. His judgment that the congestion was transient was borne out by the patient's smooth recovery after lobectomy and thoracoplasty.

The comparison of series of cases would be easier and of more value if all observations were recorded according to the simple classification set up in Houghton and Joules'[26] analysis of the material studied by the British Tuberculosis Association. Bronchoscopists in the six cooperating hospitals were asked merely to report: *1.* redness (easy bleeding); *2.* gross mucosal changes (edema, granulations and active or healed ulceration); *3.* distortion or stenosis. Even with this almost elementary scheme, the positive bronchoscopies ranged from 18.7 per cent of 91 cases in one hospital to 85.3 per cent of 34 cases in another. There was no apparent explanation for the wide

spread except, as the authors observed, the difficulty of establishing a base line of normality.

Correlation of Gross and Microscopic Observations. No attempt was made in the study at Charity Hospital to determine the correctness of bronchoscopic observations in relation to laboratory and postmortem studies, but reports from the literature indicate that in this respect bronchoscopy is not yet a precise method and probably never will be.

When Wilber[21] in 1942 reported 177 cases of tracheobronchial involvement in 500 autopsies on tuberculous subjects, bronchoscopy was still being used only occasionally. It was performed in only 39 cases in her series, once in 35 cases and apparently twice in four others, with the following results: Nine cases positive for tracheobronchial disease on bronchoscopy were negative at autopsy. Eleven cases positive at autopsy had been reported negative on bronchoscopy. Nine cases were positive on both autopsy and bronchoscopy, and 11 others were negative on both examinations. Since autopsy was, as always, the court of last resort, this meant an error of approximately 50 per cent in the bronchoscopic diagnosis.

Houghton and Joules'[26] study for the British Tuberculosis Association included a bacteriologic and microscopic study of 95 resected specimens, 57 secured at pneumonectomy and 38 at lobectomy. In the pre-surgical bronchoscopic examination special attention was paid to the portion of the bronchial tree in which the resection was to be done, the findings being recorded merely as normal or abnormal. The results of the study were as follows:

In 56 cases reported as normal on bronchoscopy, there was histologic evidence of tracheobronchial disease in 53 resected specimens — 94.6 per cent. In 20 instances the disease was severe, and in 12 florid. Bacteriologically, guinea pig inoculation was positive for tuberculosis in nine of 29 bronchoscopically normal cases.

In 39 cases reported as abnormal on bronchoscopy, there was histologic evidence of tracheobronchial disease in 37 — 95 per cent. In 14 instances the disease was severe, and in 13 florid. Six of 23 guinea pig inoculations were positive.

As these observations indicate, bronchoscopic findings that are apparently normal, by no means exclude bronchial involvement, and vice versa, but the diagnostic error is much more likely to be negative than positive. A negative error, it is scarcely necessary to add, is more misleading and may be much more harmful than a positive error.

The histologic incidence of tracheobronchial disease is now being altered by the use of streptomycin therapy, a fact which should be borne in mind when both clinical and laboratory studies are made. Thus Olson and his associates[25] reported that tracheobronchial disease was present in only 99 (31.7 per cent) of 311 specimens removed from patients who had streptomycin-PAS therapy for four months or more, while 144 specimens (49.4 per cent) of 291 removed from patients who had lesser amounts of treatment were positive for disease in this area.

Differential Diagnosis. In the absence of proof to the contrary it is reasonable to assume that tracheobronchial lesions in a patient with pulmonary tuberculosis are tuberculous lesions. This was not always the opinion, and certain other conditions, naturally, must still be considered in the differential diagnosis.

Syphilis is considerably less important now than it was 20 years ago. Carcinoma of the lung, because of its greatly increased general frequency, is considerably more important. It was present in one (fatal) case in this series, in which the pneumonectomy performed was on the indication of bronchogenic carcinoma and not tuberculosis. Boyce,[33] in his studies on fatalities from carcinoma of the lung at Charity Hospital of Louisiana at New Orleans, has called attention to the disastrous consequences which may follow concentration upon pulmonary tuberculous disease to the exclusion of possible malignant disease.

The association of carcinoma of the lung and pulmonary tuberculosis is estimated at about 1 per cent, and the association of all carcinomas and pulmonary tuberculosis at about 3 per cent. One other patient in this series had a fatal nasopharyngeal carcinoma, with extensive metastases, and another,

who was living when last heard from, had a carcinoma of the breast. The incidence of associated malignancy in this series is, therefore, not too far out of line with the general estimates.

It might be added that two of the three diabetics in these 200 cases were in the bronchoscopically positive group. Both died. There were also two alcoholics in the series. Both of these conditions greatly increase the difficulty of treating pulmonary tuberculosis and its complications.

COLLAPSE THERAPY IN TRACHEOBRONCHIAL DISEASE.

One fact which became evident when tracheobronchial disease first began to be understood has become increasingly evident as the use of bronchoscopy has increased: it is that many failures of collapse therapy which were formerly regarded as inevitable and unavoidable are actually due to the existence of this complication. As Eloesser[7] noted in 1934, and as many reported cases, including some in this series, are still proving, many patients with tracheobronchial disease can be treated by collapse therapy without harmful results. The risk is always present, however. It is never clear in advance in which cases the results may be good and in which disastrous.

The blind use of collapse therapy, whether nonsurgical or surgical, is, therefore, not justified. When it is employed in the face of tracheobronchial disease, the post-therapy course is frequently stormy. Collapsed lungs often remain unexpandible. The primary disease often spreads to the previously intact contralateral lung. It is true that the introduction of potent antibiotics has greatly reduced the incidence and lethality of such complications as empyema, but that is no justification for the violation of sound surgical principles.

The risk of collapse therapy in tracheobronchial disease can be explained on an entirely mechanical basis in all cases, though in the individual case the anatomic alterations and subsequent pathologic changes are modified by the acuteness and extent of the tracheobronchial involvement, and by the degree of stenosis already present and further induced by the collapse procedures employed. All collapse procedures produce relaxation and shortening of the bronchi, with more or less

angulation. All of them, therefore, produce some degree of obstruction if it is not already preesnt; increase whatever stenosis may already exist, and encourage stagnation of secretions.

It is generally agreed that pneumothorax is the worst offender in this respect and thoracoplasty the least. Keers,[24] perhaps, had this in mind when he said, in his 1953 presidential address to the Tuberculosis Society of Scotland, "that in the whole history of medicine there was probably no procedure which, since its introduction, had been so often misapplied and had been attended with so many serious, long-term complications."

If pneumothorax has been carried out in the presence of tracheobronchial disease of any consequence, distal angulation of the bronchial tree occurs on the affected side. The so-called check-valve effect of a kinked bronchus often explains a cavity which continues to enlarge in spite of an apparently successful collapse. If adhesions are severed after pneumothorax, the distortion of the bronchial tree is increased. Bernstein[25] reported from a Veterans Administration hospital that pneumothorax was employed in 24 of 43 cases of tracheobronchial involvement and was unsuccessful in all 24.

Both phrenic interruption and pneumoperitoneum act by lifting the dome of the diaphragm. As a result, pressure is exerted against the bronchial tree from below. If the elevation is excessive, dorsal angulation in the left main bronchus is greatly increased and its lumen, as well as the orifice of the upper lobe bronchus, may be reduced to a mere slit.[27] The existence of an endobronchial lesion in these circumstances could well spell disaster. On the right, although there is buckling of the main bronchus at the level of the orifice of the middle lobe bronchus, it is less significant.[27]

Phrenic interruption has another deleterious consequence when it is used in the presence of tracheobronchial disease. Since it paralyzes the diaphragm, it further encourages the stagnation of bronchial secretions.

The wisest plan, when tracheobronchial disease exists, is to defer all collapse therapy until it is controlled. If for any

reason the internist considers it imperative to act at once, thoracoplasty does the least harm. This operation is relatively safe if it is performed in the face of relatively mild involvement of the bronchial tree. If, however, it is performed for disease of the right upper lobe, the distortion is extreme: the superior angulation of the normal bronchus is brought down, so that it is sometimes possible to look directly down the right upper lobe bronchus and even to visualize some of the tertiary branches.[27]

CLINICAL AND ROENTGENOLOGIC VERSUS BRONCHOSCOPIC DIAGNOSIS.

Clinical Considerations. A wheeze is generally regarded as the most important and most characteristic clinical observation in tracheobronchitis, but various observers have found other symptoms and signs important. In Acuña's[22] series, for instance, the patients complained, variously, of subjective pressure on the anterior chest wall, difficulty in raising sputum, rhonchi, an asthmatoid wheeze sometimes audible at a distance, snoring and a subjective sensation that a foreign body was caught in the trachea.

Physical findings included flatness on percussion of the interscapular area, subcrepitant rales, and circumscribed areas of atelectasis or emphysema. Heaf,[3] whose observations were limited to patients with tracheal disease, mentioned a loud, distressing paroxysmal cough, very refractory to treatment; deep-seated retrosternal pain; a raw, aching sensation across the chest after a bout of coughing; a feeling of tightness across the chest; and limited sputum. The prominent pulmonary change at autopsy was fibrosis.

Our findings, from the clinical standpoint, are much more in accord with that of Flance and Wheeler.[17] Although they regarded their records as fairly accurate, their patients showed no marked wheezing, dyspnea, cyanosis or changes in the sputum beyond that which would be attributed to a terminal stage of the disease.

In this series, the sputum was positive in 60 of the 66 cases of tracheobronchial disease, but otherwise the clinical

picture was not characteristic. It was, in fact, chiefly the picture of basic tuberculosis, with fever, cough and hemoptysis the most prominent symptoms. A wheeze was present in only 13 cases in the whole series; in seven of these there was no endobronchial involvement, while in only one was the disease stenotic in character. For what it is worth, it might be said that there were three fatalities in these 13 cases.

The important consideration is not the symptoms and signs which are or are not present in tracheobronchial tuberculosis. It is the inability of even astute and experienced internists to make the diagnosis by clinical methods. In the 121 bronchoscopically positive cases collected by the Research Committee of the British Tuberculosis Association[26] there was clinical evidence of disease in 48 (37 per cent), the incidence at the six cooperating hospitals ranging from 14 to 70 per cent; but there was also clinical evidence of the disease in 36 of 255 normal cases — 14 per cent. The interpretation of symptoms and signs varied widely and showed clearly that clinical assessment is not a reliable guide to diagnosis. Jarman's[6] experience was to the same effect: when a presumptive diagnosis of present or absent tracheobronchial disease was made on clinical grounds, it was 51.5 per cent correct in the bronchoscopically positive cases and 86.3 per cent correct in the negative cases.

Roentgenologic Observations. Roentgenologic observations are no more reliable in the identification of cases of tracheobronchial disease than are clinical observations. As all workers in the field of pulmonary tuberculosis know, bronchial stenosis may occur without roentgenologic evidence of atelectasis, and complete roentgenologic stenosis may be observed in a patient who gives no clinical evidence of what has occurred. On the other hand, Wilson's[31] statement is probably correct, that if careful X-ray observations are added to careful clinical observations in the selection of cases of pulmonary tuberculosis for bronchoscopy, the incidence of tracheobronchitis should be at least 50 per cent.

Most of the roentgenologic findings which may indicate tracheobronchial disease were present in the 200 bronchoscoped patients studied at Charity Hospital (see Fig. 9). They

were present, however, with much the same frequency in both bronchoscopically positive and bronchoscopically negative cases. Certainly there were no findings in either group which would warrant the diagnosis of tracheobronchial involvement or its exclusion on roentgenologic findings alone.

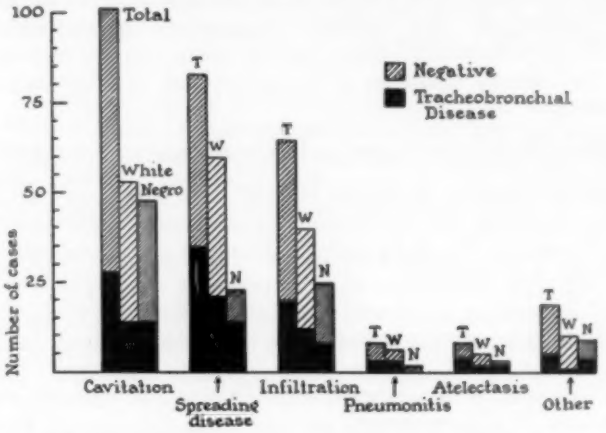

Fig. 9. Roentgenologic observations in 200 bronchoscopically studied cases of pulmonary tuberculosis, Charity Hospital, 1946-1953.

Examination of Fig. 9, in which the observations are overlapping, shows that cavitation was the most frequent roentgenologic finding. It occurred in 48 of the 79 negroes, and in 53 of the 121 white subjects studied. Cavitation is a predominant characteristic of pulmonary tuberculosis in the negro.

The literature emphasizes that cavities of certain types are likely to be present in tracheobronchial disease. The list includes those which increase in size with pneumothorax or which do not close when pneumothorax is otherwise successful; those which appear and disappear or which vary in size from time to time; those which show fluid levels; those which are large and round or which have thin walls; and those which are located in the hilum. The cavities observed in the roentgenograms in this series showed, *in toto*, most of these characteristics, but this was not differentially helpful. The

same findings were present in both bronchoscopically negative and bronchoscopically positive cases and their presence, therefore, was not a reliable index of the presence or absence of tracheobronchial disease.

In stenotic disease, it might be added, fluoroscopy is frequently helpful in the selection of the cases which should be bronchoscoped. The presence of areas of trapped air is a positive indication for bronchoscopic study, though the absence of such areas, again, is no indication that the disease is not present.

INDICATIONS AND CONTRAINDICATIONS FOR BRONCHOSCOPY.

In the light of what has already been said, there need be little discussion of the indications and contraindications for bronchoscopy in pulmonary tuberculosis. There are two general indications:

1. Bronchoscopy should always be performed in the presence of symptoms, physical signs or roentgenologic findings suggestive of the disease. These include a unilateral wheeze; positive sputum inconsistent with clinical and roentgenologic evidence of improvement; marked variations in the volume and character of the sputum; alternating positive and negative sputum; expectoration of fibrin plugs or mucus casts, which are suggestive of ulcerative disease;[31] persistently positive cultures from gastric washings without evident roentgenologic explanation; spreading disease; dyspnea out of proportion to the reduction in the vital capacity; fever, including persistent fever after thoracoplasty; atelectatic and obstructive pneumonitis; a sudden increase in the X-ray shadows about a previously stable focus.[24]

2. Bronchoscopy should also be performed, as a precautionary measure, before any collapse therapy or resectional procedure. The damage that may be done if collapse therapy is instituted in a patient with tracheobronchial disease more than justifies the time and effort required to perform bronchoscopy. This precaution is doubly important if the disease is bilateral and bilateral collapse therapy is to be instituted.

In the opinion of most observers, there are only three contraindications to bronchoscopy:

1. It should not be performed in the course of profuse hemoptysis unless bronchoscopic aspiration of blood should be indicated. The reason for this contraindication is not any possible ill effect from bronchoscopy during hemorrage, but the futility of performing a procedure which requires full vision when the field is hopelessly obscured by blood. Attempts at hemostasis by bronchoscopy are no longer regarded as of any value.

2. It should not be performed in ulcerative laryngitis, unless it is required for emergency reasons, such as sudden bronchial obstruction, because of the risk of disseminating the disease. If the laryngeal involvement is non-ulcerative, a properly performed bronchoscopy will do no harm.

3. It should not be performed in a patient so ill that he cannot tolerate the procedure at the time. Nor, for humanitarian reasons, should it be performed in a patient so near death that the information secured from the examination could not possibly benefit him. More is said on this subject under the heading of possible reactions.

TECHNICAL CONSIDERATIONS.

Except for certain precautions required by the infectious nature of the disease, bronchoscopy in tuberculosis is performed by exactly the same technique as in any other circumstances.

Anesthesia should be complete, to permit an adequate examination of the bronchial tree, but it should not be in excess of the requirements. The 200 bronchoscopic examinations studied at the Charity Hospital were performed under a combination of barbiturate premedication and topical anesthesia secured with either pontocaine or cocaine. No drug reactions were noted. Ether was occasionally used, especially in younger patients.

Daly and his associates,[24] whose 434 bronchoscopies were all performed in young children, stated that they had no difficulties in any of their cases; they used a combination of surital and local procaine. For both physical and psychic reasons young children should be completely anesthetized.

The procedure could not yield information of value if it were performed on a struggling, frightened child, and no child should be subjected to such an ordeal.

Although the great majority of the bronchoscopies performed in this series were done by residents, of course under supervision and after training, only four were listed as difficult.

All manipulations should be gentle. No attempt should be made to force the bronchoscope past an actively obstructive lesion, particularly when it is undergoing superficial necrosis; the material dislodged would almost certainly contain tubercle bacilli, and spread of the disease to a healthy part of the lung would be almost inevitable. Great care should also be used in the examination of ulcerative lesions, which are easily traumatized. The instrument should always be withdrawn slowly and deliberately. In obstructive cases the 5-mm. bronchoscope is preferable to the instrument 7 mm. in diameter.

Jackson and Jackson[32] lay great stress upon the consistent use of draperies of the same shade of green. Most observers prefer to conduct the operation in a completely darkened room, in which the color of the draperies would be of no consequence.

It would be utterly unrealistic to ignore the fact that inexperienced bronchoscopists, because they fear infection, are often less successful than they might be in the identification of tracheobronchial disease. Their apprehension manifests itself in two ways: they are inclined to stand too far away from the patient, although a satisfactory bronchoscopic examination naturally requires inspection from very close at hand. Much more often, they seem to work on the principle of getting in and getting out as fast as possible. An examination conducted on this basis is also unsatisfactory. Bronchoscopy must be a deliberate procedure.

This candidate has found that the beginner will promptly correct his ways if it is pointed out to him that the risk in tuberculosis is not from patients who are known to have the disease, and in whose examination the proper precautions will be taken, but from patients who are not known to have it. A known risk, in short, is seldom a risk of any consequence.

The bronchoscopist, however, must never relax his precautions against infection. This is a careless error which the more experienced operators are likely to commit. A strict aseptic routine must be followed. Most hospitals provide some sort of protection in the form of a mask, like a welder's mask, and it should always be used. A double mask of heavy gauze should also be worn over both the mouth and the nose.

The collection and examination of secretions may furnish useful information, particularly in cases in which the disease is suspected but the clinical picture is inconclusive and the sputum is negative. It is unfortunate that these studies are not made more often. Tubercle bacilli were identified in the only case in this series in which they were employed.

Bronchoscopic biopsy was fairly common when tracheobronchial disease was first coming into prominence. It was generally discontinued because of the risk of invasion of normal tissue, spread of infection, and delayed healing of the incision, which far out-weighed the possible information to be gained by it. These objections are of less consequence since the introduction of the antibiotics, and biopsy is again beginning to be used in carefully selected cases. Its rationale is evident when the high percentage of histologic disease not diagnosed grossly is recollected. Biopsy was used in only two cases in this series, and rather half-heartedly in them.

Serial Bronchoscopy. Serial bronchoscopy has a double field of usefulness. If the original observation is negative but there is a strong suspicion that tracheobronchial disease exists, the wisest plan is to withhold definitive treatment for several weeks and then repeat the bronchoscopy. Repeated observations yield a small but definite percentage of positive cases.

The second indication for serial examination, to follow the progress of an endobronchial or tracheobronchial lesion, was present in 22 cases in this series, in which 55 bronchoscopic examinations were made. Resectional therapy was eventually carried out in 17 cases. The majority of the patients were bronchoscoped only twice, but one patient had five bronchoscopic examinations.

REACTIONS TO BRONCHOSCOPY.

One reason given by some internists for their failure to employ bronchoscopy in patients with pulmonary tuberculosis, no matter what information might be derived from it, is fear of spreading the disease. Neither personal experience nor a review of the literature warrants this fear. Radner,[36] who is almost alone in his experiences to the contrary, made a search of the American literature in 1943 and found only 11 cases in which a spread of the disease followed this procedure. In view of the thousands of bronchoscopies which had been performed by that date, this does not seem an excessive number, even granting that in every instance the spread of the disease was a direct result of the bronchoscopy, which does not follow. In the 200 cases studied in this series, there was no instance of a sudden rise of temperature, hemoptysis, unexpected clinical or roentgenologic evidence of spread, or any other indication that the procedure had been harmful.

Alexander,[37] whose voice will always carry authority, found the reaction of the tuberculous subject no different from that of the nontuberculous subject, and thought the worst possible sequela was a sore throat for a day or two, if that. McIndoe and his associates[16] reported that 45 of their 272 patients had transient changes in the larynx and 49 had mild febrile reactions, none of any significance. Four patients had an increase in pulmonary disease, but these observers did not think that it was necessarily the result of bronchoscopy.

Houghton and Joules[26] analyzed their 251 cases from the standpoint of possible reactions, finding no roentgenologic evidence of spread in any case, and a transient rise of temperature (above 99°F. for three days) in only three cases — 1.2 per cent.

Coates[38] in 1948 reported on 473 bronchoscopies carried out on 233 patients at Trudeau Sanatorium over a 10-year period. He found the increase in parenchymal disease in these cases in the two-month period after bronchoscopy to be no greater than in the preceding two-month period. Atelectasis occurred in only one of the 73 cases in which an increase of the disease after bronchoscopy was noted. His conclusion, that the skill

of the operator plays a large part in the incidence of reactions, is perfectly sound. At Trudeau, of course, bronchoscopic skill is of a consistently high standard.

Radner,[26] as already mentioned, is alone in the high percentage of reactions reported after bronchoscopy. Fifty-three of 97 patients, who were examined 73 times at the Leahi Hospital in Honolulu, presented no deviation, clinically or otherwise, from the expected course. The other 44 patients who were bronchoscoped 110 times, showed more or less significant deviations. Eighteen had transient immediate rises of temperature, which were regarded as of no consequence, but 26 had secondary rises, all between the tenth and sixteenth days, and all lasting from 14 to 21 days. In 21 of the 44 cases, roentgenograms showed a minimal infiltrative spread, and in five cases there was atelectasis of a part of a lobe or an entire lobe.

Whatever may be the explanation of these unusual observations, the precautions which Radner recommends could profitably be followed. One is that bronchoscopy be performed at least three weeks before any contemplated surgery, and that a repeat film be made just before operation. This will make it possible to distinguish between spread of the disease resulting from bronchoscopy and spread resulting from surgery. Another precaution is that six to eight weeks be permitted to lapse between bronchoscopic examinations, to avoid possible overlapping reactions. Radner is correct in his emphasis upon the importance of the prompt return of the cough reflex after bronchoscopy, though this candidate does not share his opinion that positioning is helpful.

That most observers consider a correctly performed bronchoscopy to be associated with only minimal risk does not, of course, mean that accidents do not happen. One of Acuña's[22] patients, for instance, died of (proved) morphine poisoning. Another of his patients, with bilateral disease of the fibrostenotic type, became extremely dyspneic during the procedure and required oxygen. Two of Hawkins'[18] 516 patients, both chronic asthmatics, developed cardiac depression, but both recovered promptly.

Three of Hawkins' patients died within three weeks, of bronchoscopy. Two patients in this series died within

a week. None of these five deaths could be directly related to the bronchoscopic examination, but there was no justification in any of the cases for employing the procedure. These patients were obviously close to death. When bronchoscopy can provide no information which would be useful in the management of the patient, as it obviously could not in these cases, it should not be performed. Its employment to secure information of purely academic interest is totally unjustified and is not in line with humane medical practice.

THERAPY.

An analysis of therapy is scarcely the business of a bronchoscopist. He will, however, fulfill his function with more interest and efficiency if he understands the indications for the various types of procedure and if he can follow up the results. The data on the prebronchoscopic and definite management of these 200 cases are presented in the light of that philosophy.

Before bronchoscopy, active surgery in these cases was chiefly in the form of collapse (see Fig. 10). Forty-three of the 66 patients with endobronchial disease were treated by surgical collapse, and 42 (there is considerable overlapping because therapy was often multiple) were treated by nonsurgical collapse.

Raffery[39] has pointed out that parenchymal disease and endobronchial disease present two separate therapeutic problems. The manner in which the parenchymal disease is managed, he says, probably has little effect on the bronchial disease; but the bronchial disease may so complicate therapy directed to the parenchymal disease that it may have a profound effect not only on the parenchymal lesion but on the patient as a whole. One of the ways to prevent such complications is to identify existing bronchial disease before therapy is undertaken. It seems fair to say that 46 of the 66 patients in this group were put into unnecessary jeopardy by the performance of collapse therapy before bronchoscopic investigation of the status of the tracheobronchial tree.

Definitive Therapy. In some of the recent literature there has been a good deal of emphasis on the so-called target point

of therapeutic result, which is the ideal to be reached before any surgery is undertaken in pulmonary tuberculosis. The objectives include sputum conversion, roentgenologic improvement or a stationary status, and cavity closure. This candidate has been told that at the 1954 meeting of the American Trudeau Society, Samson suggested that a healthy bronchial

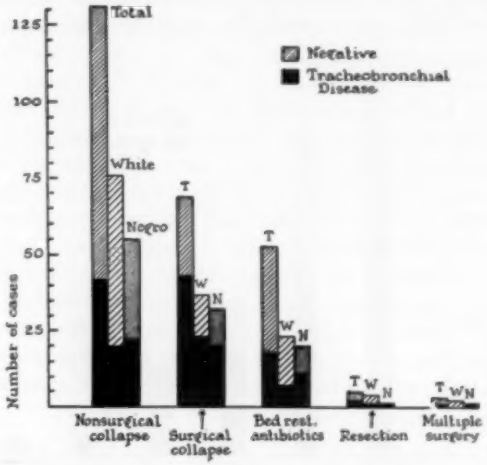

Fig. 10. Pre-bronchoscopic therapy in 200 cases of pulmonary tuberculosis, Charity Hospital, 1946-1953.

tree be added to these objectives. This is a sound suggestion from an authority who deserves to be listened to with respect in anything connected with tuberculous tracheobronchitis.

The ideals just described are not always reached in any variety of surgery. Certainly they are not always reached in the surgery of tuberculosis. They were not reached in many of the cases in this series. Criticism, however, would not be justified. In some cases there was undoubtedly a careless disregard of the existence of tuberculous tracheobronchial disease. In some there was clearly a reliance on the ability of modern antibiotic therapy to prevent complications, a reliance that did not always prove justified. The majority of the questionable or borderline cases, however, seemed to fall into

the group of desperate risks described by Overholt and Wilson[12] in their first report on resectional therapy: for these patients, who were steadily going down hill under more conservative measures, it was radical surgery or death.

Collapse therapy, which is a tissue-sparing operation, is naturally to be preferred whenever it can be performed, but in the cases of endobronchial involvement in which repeated febrile attacks occur and the sputum continues positive,

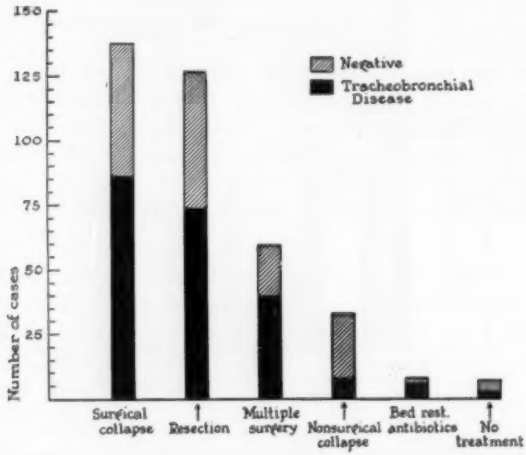

Fig. 11. Definitive post-bronchoscopic therapy in 193 cases of pulmonary tuberculosis, Charity Hospital, 1946-1953.

lobectomy and pneumonectomy, in spite of their risks, seem to have a definite if limited field. These considerations must be borne in mind in examining the distribution of definitive therapy in the cases in this series (see Fig. 11).

In 1945, when Overholt and Wilson[12] made their preliminary report on resectional surgery, penicillin was the only antibiotic available, and its use was then limited almost entirely to the military. The field of all surgery has been expanded and made safer by the present general availability of this and other agents, including streptomycin, which is now part of the standard routine of therapy in pulmonary tuberculosis. All

patients at Charity Hospital in New Orleans, who are to be submitted to surgery are now treated from four to six months before operation, as well as afterward, with streptomycin by various routines and in combination with one or another of the newer antimicrobial agents.

The availability of streptomycin and other potent antibiotics has not, however, altered any surgical principles, and their use does not compensate for failure to use all possible precautionary measures before surgery. In other words, the fact that streptomycin is effective in tuberculosis does not justify the failure to search for endobronchial disease by bronchoscopy before surgery is undertaken. That this particular complication can be entirely eliminated by this agent, in spite of its effectiveness, is doubtful; furthermore, and paradoxically, streptomycin can produce the very complication that it sometimes prevents. Healing with stenotic scarring is now a proved possibility in streptomycin-treated cases of tracheobronchitis. As Judd[40] warns, forgetfulness of this possibility might mean overlooking impending bronchial strangulation, which could be fatal. There seems no reason to take for granted that this catastrophe might not happen in the patient with tracheobronchial disease before it has been controlled.

End-Results. The five deaths in the group of patients without tracheobronchial disease and the six in the group with tracheobronchial disease need no special discussion. Two patients died within a week, before any therapy could be instituted; as already mentioned, they should not have been bronchoscoped. There were two immediate post-operative deaths not related to the presence or absence of tracheobronchial disease. One patient died of carcinoma of the lung, one of nasopharyngeal carcinoma, and one of massive hemorrhage from tuberculosis of the bladder. The majority of these deaths were without relation to tracheobronchial disease and can be eliminated from the discussion. It might be added, however, that in Houghton and Joules'[26] study the mortality was higher for resection in patients with tracheobronchial disease than in those without this complication.

In this series there was only one surgical complication, a bronchopleural fistula, in the 115 patients without tracheo-

bronchial disease who were treated by surgery. In the 55 patients with tracheobronchial disease who were similarly treated there were five instances of bronchopleural fistula, one of empyema, and three of contralateral spread. In Houghton and Joules'[26] study of resections in two English hospitals, all the complications were concentrated in the histologically positive cases. There were four instances of fistula or empyema in 31 patients with moderate disease, eight in 34 with severe disease, and nine in 25 with florid disease. As they point out, the record may not be statistically significant, but it is not one that should be ignored from the clinical standpoint.

No attempt was made in this series to follow up the 189 patients who survived surgery or other therapy. Results of a sort, however, are available, for periods varying from three months to nine years, in 173 patients, and they are presented for what they are worth. To make the comparison between cases with and without tracheobronchitis it would be necessary to match case with case in all details. This is obviously impossible, but the crude follow-up (see Table 2) nonetheless has features of significance.

The end-results that are available leave no doubt of the greater seriousness of pulmonary tuberculosis complicated by tracheobronchial disease. There were no unimproved patients, for instance, in the 113 without demonstrable disease of the bronchial tree, but one-fourth of the 60 patients with tracheobronchial disease showed no improvement over periods of observation varying from three months to two years after treatment. Eighty-three of the 113 patients (73.5 per cent) without tracheobronchial disease were classified as having arrested disease, against 26 of 60 (43.3 per cent) in the group with tracheobronchial disease. Like the results in Houghton and Joules'[26] series, these data may be of minor statistical significance, but they are of major clinical importance.

THE FUNCTION OF THE BRONCHOSCOPIST IN PULMONARY TUBERCULOSIS.

Phelps[41] in 1936 wrote with a good deal of indignation that medical men did not appreciate the importance of such complications of pulmonary tuberculosis as obstructive em-

TABLE 2 — FOLLOW-UP TO DATE IN 173 TUBERCULOUS SUBJECTS AFTER BRONCHOSCOPY AND DEFINITIVE THERAPY, CHARITY HOSPITAL, 1946-1953.

Duration Observation	Unimproved		Improved		Arrested		All Cases	
	Positive*	Negative**	Positive	Negative	Positive	Negative	Positive	Negative
To 6 months	6		4	23			10	23
1 year	8		5	3	10	14	23	17
2 years	1		6	1	4	19	11	20
3 years			2	1	6	19	8	20
4 years			2	2		12	2	14
5 years					4	4	4	4
6 years					1	11	1	11
7 years						3		3
8 years					1		1	
9 years						1		1
Total cases	15		19	30	26	83	60	113

* Tracheobronchial disease diagnosed by bronchoscopy.
** Tracheobronchial tree negative by bronchoscopy.

physema, obstructive atelectasis and "drowned lung," and should have it constantly impressed upon them. In view of the information that could be obtained by bronchoscopy, he felt that no tuberculosis sanatorium could be said to be completely staffed without a bronchoscopist.

Whether a full-time bronchoscopist should be attached to such a tuberculous section as is operated at Charity Hospital in New Orleans is doubtful. He probably could not be kept fully occupied. The wiser solution seems to be to make the services of bronchoscopists attached to the general staff fully available to this unit.

The position of a bronchoscopist in a general hospital is somewhat different from that of a staff member in a tuberculosis sanatorium. In many senses it is a delicate one. He is a consultant. He enters a case only upon consultation and re-enters it upon the same invitation. He does not select the cases for bronchoscopy except indirectly, by general advice and force of example. He does not determine therapy, and is not usually asked to advise upon it. He merely demonstrates, as best he can, the lesions of tracheobronchial disease and gives his interpretation of what he has seen.

It is an easy matter, given these circumstances, to use the services of the bronchoscopist less often than they should be used. Routine bronchoscopies, even in a tuberculosis sanatorium, are not indicated for a great many reasons, one of them being the entirely practical consideration that there are not enough bronchoscopists to perform them. The same consideration holds in a general hospital. On the other hand, as the situation at Charity Hospital shows (see Fig. 1), the bronchoscopist might profitably be employed much more often in the management of pulmonary tuberculosis. When only 200 bronchoscopies are performed in 7,500 admissions for tuberculosis, 1,000 of which were managed surgically, it is impossible to escape the impression that a great many opportunities for useful cooperation have been missed.

Failure of cooperation, it would seem, lies on both sides. The concern of this candidate is naturally with the faults of the bronchoscopists. In questioning medical men on the

tuberculosis service, he found that one reason why they did not use bronchoscopists more often was that, while their consultations were eventually answered, there was usually a notable lack of promptness in the response; furthermore, probing deeper, he found that the consultations were frequently not answered with the willingness and enthusiasm which would encourage further consultation. Surgeons in the tuberculosis unit made much the same complaints.

These are, perhaps, not very sound reasons for not using bronchoscopy more often; they are, however, very practical ones. One of the results of such a study as this is to bring out such errors and misunderstandings.

Patients with tuberculosis would be better served if medical men and bronchoscopists cooperated more fully with each other. Even more ideal would be a unit composed of internists, surgeons and bronchoscopists, who studied the patient as a whole rather than piecemeal, as is too often the way at present. The bronchoscopist should and could have a very wide field of usefulness in pulmonary tuberculosis. He is needed for diagnosis. Whether or not he is asked to advise about therapy, therapy must be based upon the observations he reports.

The analysis of these 200 cases at Charity Hospital of Louisiana in New Orleans suggests that the bronchoscopist is not extending himself in his potential area of usefulness as he might, and as, indeed, he must if he is not to lose his status as a diagnostic endoscopist, and if patients with tuberculosis are to receive the full benefits of modern scientific therapy.

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MACROPHAGES IN AURAL SECRETIONS AND THEIR CLINICAL SIGNIFICANCE.*

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In 1953 Bryan[3] published a comprehensive investigation dealing with the cytology of aural secretions in connection with acute otitis media and mastoiditis. The most interesting points in this article were the identification of large phagocytic cells in aural smears and, in particular, the observation that a certain correlation seemed to exist between the occurrence of these cells and the clinical course of otitis.

On the basis of extensive material consisting of clinically followed cases of otitis media Bryan concluded that: "*a*. The large phagocytes are an indication of relatively severe acute otitis media and usually mastoiditis; *b*. Absence of phagocytes in the discharge of acute otitis media indicates a relatively mild illness of short duration."

In the histopathological literature, which will be reviewed later in this article, the occurrence of macrophages in the exudates of otitis media has been mentioned earlier, but Bryan is the first to stress the possible diagnostic and prognostic significance of this finding. Bryan's idea is of theoretical and practical importance, especially at present when the cytological examination of secretions is continually extending its scope also in the field of otorhinolaryngology.

In this work we have attempted to study in particular the correlation between osteolytic processes and the occurrence of macrophages in aural secretions. To obtain a wider basis for conclusions we have supplemented the clinico-cytological examinations with histo-pathological studies.

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GENERAL CONSIDERATIONS.

Metchnikoff, the founder of the theory of phagocytosis, divided the phagocytic cells into two main categories: the microphages, or polymorphonuclear leukocytes of the blood, and the macrophages, which are large cells of varying genesis and morphology. In this connection we are chiefly interested in the macrophages. Terms that are used synonymously in the literature are for example polyblasts, clasmatocytes, histiocytes, large mononuclear cells, adventitial cells, pseudoxanthom cells, foam cells, etc. As a brief summary of the descriptions presented in the textbooks of histology,[13] pathology,[1,4,7,10,11] and cytology,[21] the following facts may be mentioned:

The origin of macrophages is still an open question. It seems that they arise chiefly from the monocytes of the blood, from the histiocytes of the tissues and from the different cell types of the reticulo-endothelial system in general. All cells having mesenchymal properties may, however, assume phagocytic activity and become macrophages when needed (Möllendorff[15]).

The morphological and structural characteristics of macrophages show great variations, depending upon their function and on the type of the irritant. A detailed description is superfluous in this connection.

Under normal conditions macrophages are generally present in the tissues in very small numbers. In some physiological secretions of the organism, for example in sputum and in vaginal secretion, they are a normal finding[21]; otherwise they are found more abundantly only in connection with pathological processes under conditions in which there is abnormal destruction of tissues, and in which the general circumstances are favorable for them. In inflammatory processes they form a part of the defense action and resorptive mechanism of the organism.

According to Menkin[14] the cytological picture of an exudate is dependent upon the changes in the hydrogen ion concentration in the tissues during the inflammatory process. In his monograph dealing with the dynamics of inflammation he writes:

The usual cellular sequence in the development of an acute inflammatory reaction consists of an initial infiltration of polymorphonuclear leukocytes which is subsequently replaced by an abundance of macrophages. The underlying mechanism involved in this basic phenomenon depends on the production of a local acidosis in the inflamed area. At a pH varying between 7.2 and 7.4 the predominating cell of an exudate is the polymorphonuclear leukocyte. Between 7.0 and 6.8 the macrophage constitutes the chief cellular element. Concomitant with the rise in hydrogen ion concentration, the polymorphonuclear leukocyte manifests various signs of degeneration, injury, or necrosis. Below a pH of 6.7 or thereabouts, all types of cells are injured and a state of frank suppuration ensues.

REVIEW OF THE OTOLOGICAL LITERATURE.

In his article Bryan presented a detailed review of the cytological investigations of aural smears as well as of the reports of macrophages in aural tissues under normal conditions; therefore we confine our review to the investigations dealing with the occurrence of macrophages in the middle ear during inflammatory processes.

Goerke[8] was probably the first who paid attention to these cells. In his histopathological investigation he stated that, in addition to the usual cells found in pus, the inflammatory exudate of the middle ear contains large mononucleated cells and multinucleated phagocytic giant cells. Manasse[12] spoke of "Korbzellen" and Doederlein[6] of "gedunsene Exsudatzellen," mentioning also the occurrence of multinucleated giant cells. Singer,[20] however, seems to have been the first to identify these cells as macrophages and to present a detailed study concerned with their occurrence in the middle ear; their origin, and their morphological and structural characteristics, as well as their function. According to his report, macrophages are an essential element in the inflammatory reaction of the subepithelial tissue in the middle ear.

On the basis of animal experiments he stated that this reaction takes place very rapidly. Macrophages, however, are most abundantly seen at the later stages of inflammation, when the process of healing begins. It seems that they act chiefly as "scavengers" which phagocytose bacteria, cellular debris, and lipoid substances arising during destruction of cells, and carry them into the blood and lymph vessels, or into the middle ear cavity, from which they are removed with the aural discharge; furthermore, they probably play an important role

in the process of immunization and in the defensive action of the organism in general.

Their rapid appearance, in Singer's opinion, is due to the fact that the subepithelial tissue in the middle ear originates in the reticulum of the previous marrow spaces. This tissue thus belongs to the reticulo-endothelial system. Perhaps the absence of lymphoid structures in the mucous membrane of the middle ear is compensated in this way.

Siirala[18] found macrophages in the endolymphatic sac and duct under normal conditions, and Brunner[2], in cases of serous labyrinthitis. Brunner concluded that exudate is carried away from the internal ear, at least to a great extent, by phagocytes. In addition, he mentioned that macrophages are commonly seen in the exudate of acute otitis media.

Ojala,[16] in an investigation dealing with the histopathology of adhesive otitis, also presented some observations regarding the occurrence of macrophages in connection with otitis media. He stated that "macrophages were fairly often encountered in the exudate in cases of acute otitis in which the most active stages of exudation was apparently over."

Macrophages were also a very common finding in old epithelium-lined pseudocysts formed in the middle ear as a result of previous inflammations. In these cases there were few if any signs of active inflammation in the surrounding subepithelial tissue. It seemed that macrophages had the function of removing disintegration products from these cysts, the drainage of which was otherwise not possible.

AUTHORS' MATERIAL.

The clinico-cytological material consists of 107 cases of otitis media, 102 acute and five chronic, treated in 1954 in the wards or the out-patient department of the Otolaryngological Clinic, University of Turku. Because the main purpose of our study was to obtain information regarding the correlation between osteolytic processes and the occurrence of macrophages in the aural discharge, the series was selected to contain chiefly cases of acute otitis media which had a prolonged course, or which seemed to be severe from the beginning.

A small number (17 cases) of clinically mild cases of otitis were included for comparison. The majority of the patients were children, six months to ten years of age (59 cases). All patients with purulent acute otitis were treated with antibiotics after the bacterial strain and its resistance had been determined. The patients were kept under observation until the otitis was definitely healed. A simple mastoidectomy was performed in ten cases of acute, and a radical operation in three cases of chronic otitis.

Smears were made from the aural secretion, usually by means of puncture and aspiration of the tympanic cavity, at intervals of five to seven days, sometimes more frequently, until the inflammation healed. The smears were dried in air and stained by May-Gruenwald-Giemsa's methods. Supravital staining was not used.

A histological study of bone pieces obtained at operation was made in seven cases of simple mastoidectomy and in the three cases of radical operation mentioned above.

For additional information on the correlation between osteolytic processes and the occurrence of macrophages we reexamined the material used by one of us (Ojala) in an investigation of adhesive otitis. This series comprises 116 serially sectioned temporal bones, 35 of which showed inflammation of the middle ear suitable for the purposes of our study.

In addition, we made histological studies of bone pieces obtained at 32 mastoidectomies or radical operations performed earlier without a preoperative cytological examination of the aural discharge. We also studied numerous smears taken from the bronchial secretion (26 cases) and from pleural and peritoneal exudate (60 cases) in cases of various diseases. The purpose of this study was to compare the structural and morphological characteristics of the macrophages found in these cases, in which osteolytic processes were not possible, with those found in the middle ear. Moreover some smears taken from exudates of purulent maxillary sinusitis (five cases) were examined.

RESULTS.

1. Clinico-cytological Studies: In differentiating the cellular elements in the smears, attention was paid chiefly to the

macrophages, but other types of inflammatory cells were also recorded. The proportion of macrophages was estimated roughly. If a few isolated macrophages were revealed only on very careful search, the case was placed in the group designated in the following tables as "a few." The group "moderate" consists of cases in which some macrophages were found in almost all microscopic fields. Cases showing numerous macrophages in all microscopic fields were placed in the group "abundant."

An attempt was made at first to determine how soon macrophages appear in the exudate after the onset of otitis. For this purpose the material was grouped according to the clinical duration of the otitis at the time of taking the first smear (see Table I).

TABLE I.

THE PRESENCE OF MACROPHAGES IN THE FIRST SMEAR AND DURATION OF OTITIS AT THE TIME.

Number of Macrophages	Duration of Clinical Symptoms of Otitis				
	< 2 Days	2-4 Days	5-7 Days	> 7 Days	Together
None	14	17	2	3	36
A few		17	8	7	32
Moderate		8	6	10	24
Abundant			3	7	10
Total	14	42	19	27	102

The data regarding the duration of the clinical symptoms of otitis before the first smear were estimated on the basis of the case histories, and of course they are not always accurate. It may be said that the duration of the inflammation probably was not shorter, but especially in the cases of children, may sometimes have been longer, than the time indicated in Table I.

Table I shows that macrophages were not found in cases in which the clinical symptoms of otitis had lasted less than two days. The smears in these cases contained chiefly polymorphonuclear leukocytes. In addition, red blood corpuscles, lymphocytes and monocytes were constantly found in various numbers, and often also fairly large mononuclear cells (c. #16—20 μ diameter) with a usually eccentric, rounded or ovoid nucleus

and structureless cytoplasm without signs of phagocyted material.

Apparently these cells were histiocytes which had not yet begun their phagocytic activity. Although the material is small, and the data regarding the duration of otitis are not precise, it may be concluded that large phagocytes seldom make their appearance in the aural discharge during the first two days of otitis.

The macrophages increased in number and size with the duration of the otitis. When the symptoms of inflammation had lasted two to four days, macrophages were found in more than half the cases. The five cases with a history of more than five days, but with no macrophages in the smears, were cases of clinically mild serous or mucous otitis and will be

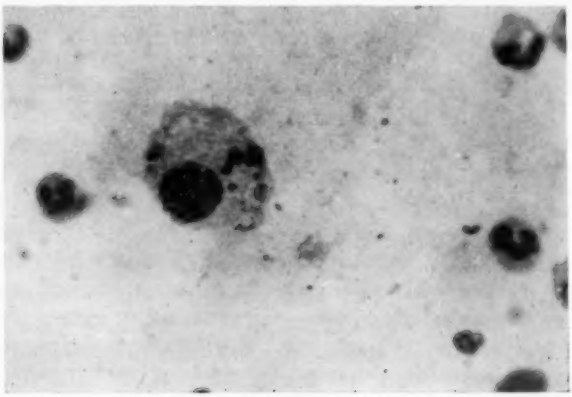

Fig. 1. In this case the symptoms of an acute otitis media had lasted two days. The smear showed a moderate number of small and medium sized macrophages, about 20-30 μ in diameter, the one seen in the microphotograph measuring 20 μ. The ear healed within a week. High power magnification.

discussed later on. On the other hand, macrophages were always found in cases of purulent otitis which had lasted more than five days when the first smear was taken. Thus our findings suggest that macrophages are a constant cellular element in the exudate of the middle ear in connection with purulent otitis media of more than five days' duration.

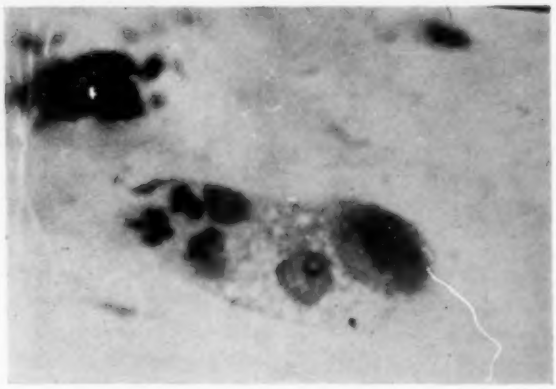

Fig. 2. The otitis had lasted 3 days before admission to the Clinic. The smears made every day revealed varying numbers of macrophages the size of which was at first fairly small, but in the later smears also very large phagocytes were found. This giant phagocyte, the largest diameter of which is about 60 μ, was found in a smear made 12 days after the onset of the otitis. Two days afterwards the ear was dry. High power magnification.

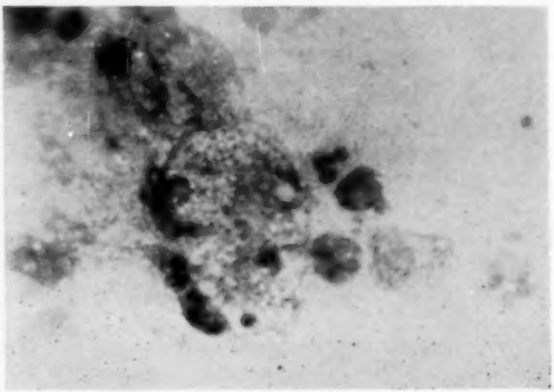

Fig. 3. The otitis had lasted two weeks prior to the admission to the Clinic. Smears made at intervals of 2 to 4 days showed macrophages, the number and size of which varied during the subsequent course of the disease. A simple mastoidectomy was performed one month after the onset of the otitis. The smear containing this large phagocyte (40 μ) was made immediately prior to the operation (cf. also Fig. 8). The smears after mastoidectomy showed macrophages in ever-increasing numbers. After 8 days the ear was dry. High power magnification.

The various morphological and structural characteristics of the macrophages are most clearly apparent in the photomicrographs (see Figs. 1, 2, 3); some clinical data are also given in the legends. In the group in which otitis had lasted two to four days the macrophages were usually small, about 20-25 μ in diameter.

Their cytoplasm contained vacuoles and/or particulate matter. In some cases also larger macrophages, about 30-35 μ in diameter, were found scattered here and there in small numbers. With increased duration of the otitis the larger macrophages become more common, but multinucleated giant cells were seldom seen in cases in which the otitis had lasted less than seven days before the smear was taken.

Table II classifies the material by the clinical type of the otitis and by the presence of macrophages.

TABLE II.
MACROPHAGES IN VARIOUS TYPES OF OTITIS.

Number of Macrophages	Type of Otitis			
	Serous	Mucous	Purulent	Together
None	6	1	29	36
A few	2	4	26	32
Moderate		2	22	24
Abundant	1	1	8	10
Total	9	8	85	102

The otitis was defined as serous, mucous or purulent, according to the otoscopic appearance of the tympanic membrane and the macroscopic and microscopic character of the exudate. In all cases of otitis defined as serous or mucous, the culture revealed no growth of bacteria. Table II shows that macrophages were found in nine of the 17 cases of serous or mucous otitis; in two cases they were abundantly present.

The case history revealed that the otitis in these two cases had begun seven and 21 days earlier respectively, the initial symptoms, fever and pain, passed, and the patients later came to treatment because their hearing did not improve.

It may be supposed, therefore, that the otitis had begun as a purulent one and was already in process of healing when the first smear was taken. In all these cases the tympanic membrane was not perforated. Clinical symptoms and signs

of mastoiditis were absent and after myringotomy the ears healed in a short time without complications.

In the seven cases of serous or mucous otitis with no macrophages in the exudate the symptoms were those of a secretory catarrh. Five of them had lasted more than five days when the first smear was taken. The exudate contained a few inflammatory cells, mainly lymphocytes and monocytes, or no cells at all. The 29 cases of purulent otitis showing no macrophages in the exudate included 14 in which the otitis had lasted less than two days, and 15 in which it had lasted two to four days.

Table III shows the correlation between the occurrence of macrophages and the clinical course of otitis in our case material.

TABLE III.

THE PRESENCE OF MACROPHAGES PLOTTED WITH RECOVERY AND CLINICAL COURSE OF OTITIS.

Number of Macrophages	Recovery within				From these with
	7 days	7-14 Days	14-30 Days	> 30 Days	Mastoidectomy
None	13	17	6		
A few	6	13	9	4	3
Moderate	1	12	5	6	5
Abundant		1	3	6	2
Total	20	43	23	16	10

The period of recovery shown in Table III was calculated on the basis of the case histories from the day of the onset of otitis to the day when the middle ear was dry, the drum membrane of normal appearance, and the hearing within normal limits. With respect to the proportion of macrophages, the cases were classified by the smear containing the largest number of macrophages. The greater part of the patients were treated in the out-patient department and checked at five to seven day intervals. A resulting disadvantage was that the ears which made a rapid recovery were usually dry at the second examination, and further smears could not be taken.

Table III shows that 30 out of the 36 ears without macrophages in the exudate made an uneventful recovery within two weeks. This statement seems to support Bryan's view that absence of phagocytes in the discharge of acute otitis media indicates a relatively mild illness of short duration.

According to case reports, there was a mild serous or mucous otitis in eight of these cases. The remaining 22 cases showed all characteristics of a severe purulent otitis at the first examination. The patients concerned came under treatment during th first few days of their illness. Apparently macrophages had not yet appeared in the exudate in these early cases (see Table I).

When the patients came to the second examination the ear was already dry, and further smears could not be made. The influence of antibiotics could not be precisely evaluated. It seems, however, that our case material does not allow such generalized conclusions as presented by Bryan. In our opinion, the only conclusion to be drawn from the absence of phagocytes in the discharge of acute purulent otitis media is that the otitis has lasted a rather short time.

Of the 66 cases with macrophages in the exudate, exactly one-half recovered within 14 days. In the other half the otitis was more prolonged, mastoidectomy being necessary in ten cases. The proportion of cases lasting more than 14 days increased, in agreement with the finding of Bryan, with the number of macrophages in the exudate. The proportion of mastoidectomies was approximately the same (about 20 per cent) in the groups showing a moderate or a large number of macrophages; it was about twice that in the group with a few macrophages. Before drawing any conclusions we wish to deal shortly with some factors which do not appear from the table.

It was stated in connection with Table I that the number of macrophages generally increased with the duration of otitis. It must be added that in many cases macrophages were most abundant immediately before healing of the otitis. We present two illustrative reports.

Case 81, a boy eight years of age, became ill two weeks previously with high fever and severe pain in both ears. The family doctor prescribed aureomycin, 750 mg. daily, for one week and did not perform myringotomy. The severe symptoms diminished, but slight fever and earache persisted, and the hearing was much impaired. During the last two days before admission the fever rose again to 39° C. The patient was sent to our out-patient department and was admitted to the wards.

The boy looked severely ill. The temperature was 38.6° C. The blood sedimentation rate was 78 mm. an hour. There was purulent maxillary

sinusitis bilaterally. The ear canals were dry, the tympanic membranes were reddish, thickened and bulged outwards. Puncture and aspiration revealed much purulent exudate from which streptococcus pyogenes was cultured. The Roentgenograms showed an extensive cell system, diffusely shadowed but with no signs of destruction of bone. In the smears macrophages were found in abundance.

The patient was treated with penicillin and streptomycin. The recovery was uneventful. The profuse discharge from both ears ceased after three days. After 10 days both drum membranes were of normal appearance and the hearing was normal.

Comment: In this case there was good reason to expect coalescent mastoiditis to develop. According to Bryan, abundance of macrophages in the exudate should also suggest such a development. The Roentgenograms, however, did not reveal signs of osteolytic processes. This negative finding was supported by the prompt recovery after proper treatment. Although the part played by the antibiotics cannot be ignored, we are inclined to believe that reparative processes were already predominating, and only adequate drainage was needed for recovery.

Case 11, a man 50 years of age. About three weeks previously the patient had a sore throat and soon afterwards experienced pain in the left ear. A general practitioner performed myringotomy and prescribed penicillin. There was a persistent slight discharge from the ear, and the hearing was impaired. Because the condition did not improve the patient was admitted to the Clinic.

The general condition of the patient was good. The blood sedimentation rate was 22 mm. an hour, and the leukocyte count 8550 cu. mm. There was a slight mucous discharge from the left ear. The Roentgenograms revealed an extensive cell system with diffuse shadowing but without signs of destruction of bone. The smears contained neutrophilic and numerous eosinophilic leukocytes, lymphocytes, monocytes, and a moderate number of macrophages. Culture did not reveal growth of bacteria.

The patient was treated with antibiotics and antihistamins for a week. There was no improvement; on the contrary the hearing grew continuously worse, and a simple mastoidectomy was performed about four weeks after the onset of otitis. The extensive cell system was filled with sero-mucous exudate. The mucous membrane was slightly edematous. There was no macroscopic evidence of destruction of bone. Microscopic examination was not performed.

The recovery was prolonged. After six weeks the ear was dry and the hearing almost normal. The smears, examined every week continued to show eosinophils and macrophages in addition to other inflammatory cells. Towards the end of the disease, the number of eosinophils decreased and macrophages increased. The last two smears contained only a few cells, almost exclusively macrophages.

Comment: In this case, the otitis apparently was in the main of allergic origin. There was no evidence of osteolytic

processes. Macrophages, however, were found in the exudate during all phases of the disease, in even greater numbers after mastoidectomy. Before the definitive healing the number of these cells increased, and at last the macrophage was the predominating cellular element in the smears.

Let us now return to Table III. Although the figures in the table seem to support the conclusion made by Bryan, *i.e.* that large macrophages are a prognostically unfavorable sign, such a conclusion apparently is somewhat beside the point. On the basis of our case material it seemed that the occurrence of large phagocytes in the exudate was a sign that the otitis had lasted a fairly long time rather than an indication of a prolonged course in the future.

There was no evidence suggesting any correlation between the quantity of macrophages and osteolytic processes. An abundance of macrophages in some cases seemed to suggest that the otitis was in the process of healing; furthermore, we could not find any type of macrophages characteristic of osteolytic processes. The same structural and morphological varieties of macrophages were found both in cases with and without osteolytic processes.

The five cases of chronic otitis in which a cytological study of aural discharge was made included three of cholesteatomatous otitis, one case of chronic otitis without cholesteatoma, and one case of simple mucosal suppuration with central perforation of the drum. Macrophages were found in one of the cases of cholesteatomatous otitis and in the case of chronic otitis without cholesteatoma. In the other cases of cholesteatomatous otitis the smears showed polymorphonuclear leukocytes, lymphocytes and an abundance of desquamated epithelial cells, which sometimes formed large syncytial masses. According to Probst and Pfalz[17] such syncytial masses of epithelial cells are a characteristic finding in the discharge of cholesteatomatous otitis.

2. Histopathological Studies. The serially sectioned temporal bones at our disposal included 56 cases which showed signs of middle ear inflammation. In 21 cases the exudate was serous and contained only some lymphocytes and monocytes or no cells whatever. The remaining 35 cases were se-

lected for more detailed examination and were divided into three main groups on the basis of the inflammatory alterations.

The first group comprised 12 cases of acute suppurative otitis media. Unfortunately, the case histories did not reveal any information regarding the duration of the inflammatory process. There was, however, some histological evidence that in seven of these cases the otitis was probably of rather short duration. In the middle ear cavities there was purulent or seropurulent secretion without any signs of incipient organization.

Haymann[9] has shown, on the basis of animal experiments, that organization of exudate in the middle ear may begin as early as during the first three to four days of inflammation. So far as these statements apply to man, the inflammation in our cases may have lasted less than three to four days. In three cases the tympanic membrane was in the process of being perforated. In the others the tympanic membrane was to some extent infiltrated with inflammatory cells, but there were no necrotic areas suggesting perforation. The exudate consisted chiefly of polymorphonuclear leukocytes. A small number of lymphocytes and monocytes were also found but no macrophages. These statements are in agreement with the results of our clinico-cytological studies.

In the remaining five cases the inflammation seemed to be more prolonged. The middle ear cavities contained numerous organization processes and purulent or seropurulent exudate. Macrophages were abundant both in the exudate and in the organized tissue.

The second group consisted of two cases of coalescent mastoiditis. Fig. 4 shows an area of intense osteoclastic resorption of bone in the mastoid air cells around the antrum. The swollen mucous membrane is strongly infiltrated with polymorphonuclear leukocytes. The cell cavities are filled with fibrinous purulent exudate containing chiefly polymorphonuclear leukocytes but no macrophages.

On the other hand, small macrophages (see Fig. 5) are seen in some neighboring air cells, in which the exudate is in

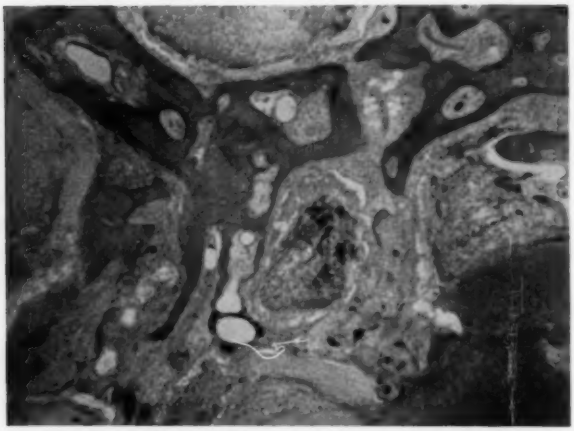

Fig. 4. Mastoid air cells in a case of coalescent mastoiditis. Macrophages were rarely if at all found in the areas of most intense osteoclastic resorption of bone. Low power magnification.

the process of organization and osteoclastic resorption of bone has changed into apposition of bone. This seemed to be the general cellular sequence. Macrophages were found very rarely, if at all, in areas where destruction of tissues was

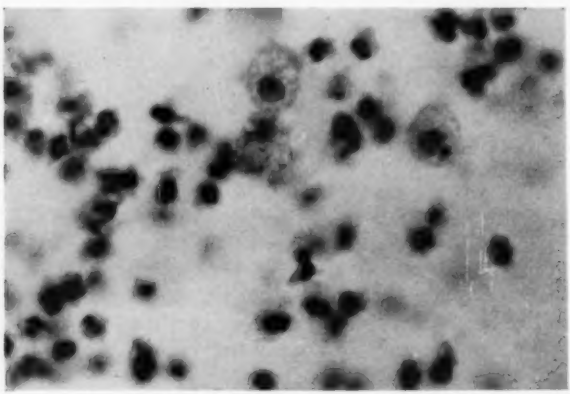

Fig. 5. The same case as in Fig. 4. Small sized macrophages in an air cell in which the inflammatory process seemed to be calming down. High power magnification.

predominant, with or without osteoclastic processes. The more prominent the signs of reparative processes, the greater was the number of large macrophages both in the exudate and in the tissues.

The third group contained 21 cases of different sequelae of otitis. In addition to old adhesions, there were in 12 cases numerous organization processes in the tympanic cavity and in the mastoid air cells. There was also serous or mucous secretion in varying amounts, and it contained numerous

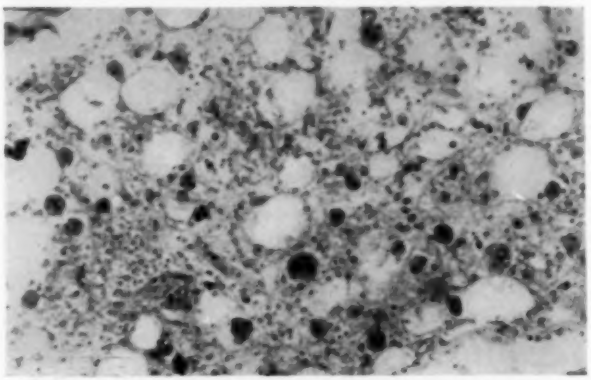

Fig. 6. Multinucleated macrophages in a marrow bone. The neighboring air cells showed abundantly organized tissue and serous exudate containing exclusively macrophages. There was intense apposition of bone. Medium magnification.

macrophages; in some cases only these cells. Macrophages were also abundant in the organized tissue, in the subepithelial tissue, and in two cases in the neighboring marrow spaces (see Fig. 6). The bony walls in these cases showed no signs of active osteoclasis; on the contrary, new bone was usually laid down.

In the remaining nine cases of this group, the tympanic cavity and the mastoid air cells contained adhesive processes and numerous epithelium-lined pseudocysts which, judging from the past histories, must have been formed years before. These cysts were usually filled with macrophages and

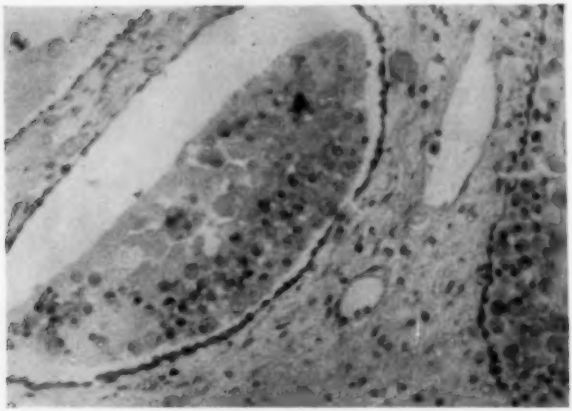

Fig. 7. Old pseudocysts in tympanic cavity containing macrophages and desquamated epithelial cells. The loose and oedematous subepithelial tissue did not show signs of active inflammation. Medium magnification.

desquamated epithelial cells (see Fig. 7). In some cysts there were also droplets of homogeneous material. It seemed possible that macrophages had the function of removing the disintegration products from these cysts.

Fig. 8. The same case the history of which is presented in the legend of Fig. 3. Numerous multinucleated giant cells (the largest measuring 59 μ) are seen in an air cell in which the inflammation obviously was calming down. The loose subepithelial tissue was to some extent infiltrated with lymphocytes and plasmacells. The bony walls showed slight apposition of bone. Medium magnification.

Histopathological study of bone pieces obtained by mastoidectomy and radical operation revealed findings which were in keeping with those reported above. The series of mastoidectomy consisted of 16 cases of acute otitis; seven of these belonged to our clinico-cytological material. Macrophages were most numerous in the air cells in which the inflammatory process was obviously calming down (see Fig. 8). In the areas of active destruction of tissues macrophages were encountered rarely if at all.

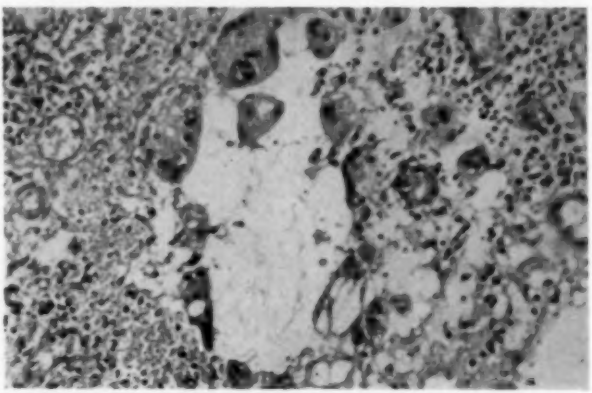

Fig. 9. "Foreign body" giant cells in granulation tissue in a case of chronic cholesteatomatous otitis. Medium magnification.

The series of radical operation comprising 17 cases of cholesteatomatous otitis and six cases of chronic otitis without cholesteatoma, showed similar results. It should be added that, besides other types of macrophages, large "foreign body" giant cells were a very common finding in these cases (see Fig. 9). Usually they surrounded slits in the granulation tissue. Evidently these slits had contained cholesterol or fatty acid crystals, which had resolved during preparation. The occurrence of such giant cells in connection with chronic otitis has been mentioned earlier, for example by Drennova[8] and Simonetta.[19]

From these results it may be concluded that the occurrence of macrophages, in cases with and without osteolytic processes, is mainly linked up with the reparative and resorptive functions. In coalescent mastoiditis reparative and destructive processes alternate, and there are always areas in which either one or the other of these processes predominates. The macrophages occurring in the exudate of coalescent mastoiditis are obviously derived mainly from areas where reparative processes predominate. There is no evidence for the assumption that an abundance of macrophages in the exudate of otitis media might be a sign of unfavorable prognosis. In fact, our clinico-cytological and histopathological studies seem to indicate rather the reverse.

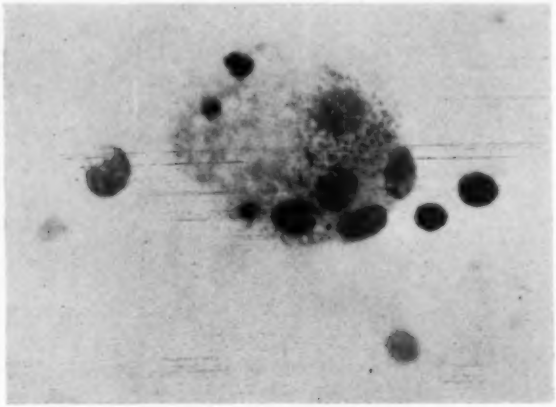

Fig. 10. Large multinucleated giant cell in bronchial secretion. High power magnification.

3. Other Cytological Studies. Bronchial secretions were secured during a diagnostic bronchoscopy in 26 cases of specific or unspecific inflammation, or of suspected malignancy. All the smears contained some, mostly numerous, small or medium sized macrophages, 15 to 25 μ, showing various amounts of phagocyted dust particles ("dust cells"). Larger giant phagocytes, 25 to 75 μ, were seen with phagocyted cellular debris or particulate matter in 17 cases of long-standing pulmonary infection (see Fig. 10). The appearance of these

cells was indistinguishable from those encountered in aural smears.

Pleural and peritoneal exudates were obtained by puncture and aspiration and stained, like the bronchial washings, by the Papanicolaou technique. The 28 pleural exudates were mostly associated with infectious disease, the 22 peritoneal fluid specimens with a condition of cirrhotic liver or suspected malignancy. In these smears lymphocytes and monocytes were frequently seen. Giant phagocytes were clearly more scarce than in bronchial aspirations. Nevertheless, typical large phagocytes with ingested cellular debris were found in six pleural and four peritoneal specimens.

All of the five cases of purulent maxillary sinusitis, in which the exudate was studied cytologically, were complications of acute rhinitis and, judging from the clinical symptoms, had lasted about one or two weeks. The smears contained chiefly polymorphonuclear leukocytes. Macrophages were not found, although they were very carefully sought.

DISCUSSION.

Our studies showed that the usual cellular sequence in inflammations of the middle ear follows the general lines described by Menkin. For the first few days of acute suppurative otitis the polymorphonuclear leukocyte is the chief cellular element in the exudate. It seems that active macrophages seldom make their appearance in the exudate before the otitis has lasted about two days. After about four days they seem to be a constant finding. They increase in number and in size with the duration of otitis and, before healing of the inflammation, they may become the predominating cellular element in the exudate.

Unfortunately, we could not determine the pH of the exudate, the lowering of which, according to Menkin, is responsible for the changes in the type of inflammatory cells. We can only confirm the statement made by Singer, that the occurrence of macrophages is intimately connected with the general defensive, reparative, and resorptive actions of the body and, therefore, is dependent on the extent of inflammatory damage to the tissues. In very mild catarrhal inflamma-

tions with little or no destruction of tissues macrophages are not found. On the other hand, they are always found in the later stages of inflammation involving damage to the tissues whether or not there are any osteolytic processes.

On the basis of our studies there are no types of macrophages specific to inflammations of the middle ear only, nor is there any type of macrophages specific to osteolytic processes. As a matter of fact, the macrophages found in the exudate of a coalescent mastoiditis apparently are not derived from the areas of active osteoclasis but from those in which reparative processes predominate; therefore the quantity and the quality of the macrophages in the exudate of an otitis media obviously do not offer any reliable basis for conclusions regarding the presence of osteolytic processes or regarding the course of the otitis in the future.

A great number of macrophages may be a sign of extensive damage to the tissues but, at the same time, it seems to indicate that the destructive process is already calming down. A few or absent macrophages in a severe acute otitis may indicate that the inflammation has lasted a rather short time, or possibly that there is an acute exacerbation. On the whole, the diagnostic and prognostic significance of macrophages seems to be fairly limited. Perhaps it may be said that an ever-increasing number of macrophages in successive smears may be a prognostically favorable sign. Variation in the number of macrophages may indicate repeated acute exacerbations being thus, perhaps, a sign of unfavorable prognosis.

SUMMARY AND CONCLUSIONS.

This study was stimulated by Bryan's interesting investigations regarding the diagnostic and prognostic significance of large phagocytes in the exudates of otitis media. According to Bryan, large phagocytes indicate a relatively severe acute otitis media, usually with mastoiditis, while the absence of phagocytes indicates a relatively mild illness of short duration.

The present paper is based on clinico-cytological and histopathological studies. The series studied cytologically comprises 107 cases of clinically followed otitis media; furthermore,

smears of bronchial secretions and pleural and peritoneal exudates were examined in 86 cases of various diseases. The purpose of this latter study was to compare the structural and morphological characteristics of the macrophages found in these cases, in which osteolytic processes were not possible, with those found in the exudates of otitis media. In addition, cytological examination of the exudate was made in five cases of purulent maxillary sinusitis.

The histopathological material consists of 35 serially sectioned temporal bones with various inflammations of the middle ear and of bone pieces obtained at 16 mastoidectomies and 23 radical operations.

The results of the investigation allow the following conclusions:

1. The cellular sequence in connection with inflammations of the middle ear does not differ from that described in connection with other inflammations in the organism. After the first few days the macrophage is a constant cellular element in the exudate of purulent acute otitis media.

2. There is no type of macrophage characteristic of inflammations of the middle ear only, and also no type characteristic of osteolytic processes. The macrophages found in the exudate of coalescent mastoiditis are chiefly derived from the areas in which reparative processes predominate.

3. The quantity and quality of macrophages in the exudate of an otitis media obviously do not offer any reliable basis for conclusions regarding the presence of osteolytic processes or regarding the course of the otitis in the future.

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TRANS-INCUDAL STAPEDOLYSIS FOR STAPES MOBILIZATION IN OTOSCLEROTIC DEAFNESS*

(Under Audiometric Control).

A Surgical Technique for Improvement of Hearing in Otosclerosis Is Described, Utilizing New Methods In the Stapes Approach.

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Los Angeles, Calif.

SURGICAL PHYSIOLOGY OF TRANS-INCUDAL STAPEDOLYSIS TECHNIQUE.

1. Methodical lysis of stapedial footplate ankylosis by either simple rocking or mechanized vibratory force, under *operative audiometric control.*

2. Avoidance of incudo-stapedial joint dislocation by use of trans-incudal force; force is not applied to the neck of the stapes, but to the capitulum through the lenticular process of the incus. In very loose incudo-stapedial joints, preliminary immobilization of this joint is obtained by cementing with a plastic material.

3. Avoidance of surgical crural fracture by preliminary stapediotenotomy to eliminate counter pull by stapedial tendon, in cases where tendon is under tension.

4. Avoidance of unnecessary manipulation when microscopic examination and palpation reveal pathologic crural atrophy and footplate replacement by pathologic otosclerotic bone.

HISTORY.

That "ankylosis" of the stapes footplate can produce a conductive type of deafness has been known for over a century. Kessel,[1] in 1876, began the surgical saga of attempts at lysis of

* The term "stapedolysis" seems useful in that it expresses a procedure aimed at "lysis" or freeing of adhesions around the stapes. This is the objective of the surgical procedure and the one word simplifies the description of the surgical objective.

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the fixed stapedial footplate. He was followed by many otologists who sought surgical techniques to reopen the closed pathway of perilymphatic sound conduction to the basilar membrane. Many names should be mentioned in this connection. It is not within the scope of this paper to go into details of this rather fascinating chapter in medical history. Blake,[2] Jack,[3] Miot,[4] Holmgren[5] and many others were identified with attempts at recreation of an acoustically mobile perilymphatic pathway to the organ of Corti.

Most of the attempts of these early surgical investigators apparently resulted in failures, although some individual brilliant successes were reported sporadically towards the end of the last century. It is surprising that some of the favorable early reports were not followed up by long range studies; however, it should not be inferred that this lapse was necessarily due to bad results. Medical history is replete with examples of discontinuity in the flow of clinical knowledge.

Whatever the causes were, the surgical approach in otosclerosis was transferred to the vestibular labyrinth shortly after the turn of the century. Early failures in this new story of *fenestration surgery* were also discouraging. The researches of Holmgren,[5] the persistence of Sourdille[6] and the final brilliant technical achievements of Lempert[7] brought to surgery for the first time a practical method for restoration of hearing in otosclerosis by fenestration of the external semicircular canal; nevertheless, the possibility of direct approach to the ankylosed stapes continued to intrigue some otologists.

Rosen's[8] recent reports on stapes mobilization have been most encouraging, and have again turned the interests of otologists back to the stapedio-vestibular articulation.

Recent surgical experiences in this field have prompted me to suggest a technique which appears advantageous and which has yielded encouraging primary results in both ideal and fair candidates for surgical intervention in "otosclerosis."*

* In this paper the term "otosclerosis" is used in the context of "clinical otosclerosis"; a term frequently encountered in fenestration literature. I conceive of this term as describing footplate ankylosis probably by a variety of pathologic states, one of which is the typical "histologic otosclerosis," as described by Wittmaack,[9] Guild,[10] Wolff,[11] Nager[12] and many others. Clinical evidence is accumulating, which points to the probable existence of lesions other than the classic "herde" of histologic otosclerosis, in the production of footplate ankylosis.

It is not within the province of this communication to deal with these results. The periods of observation are too short to permit sober evaluation. Such evaluation will be presented in a further paper, when sufficient time has elapsed for proper study of *long term* results. The specific details in this technique are based upon preliminary studies of earlier failures and upon basic physiologic principles in labyrinthine and intra-tympanic surgery.

There is sufficient evidence at this time to indicate that present technical improvements in stapes surgery may possibly produce results which might have permanent value. No such proof has yet been offered to the profession in any long range clinical case material; nevertheless, it is certain that many otologic surgeons wish to study this approach, and it is hoped that some of these technical suggestions may be useful. Undoubtedly, much of what appears in this technique will require change, and additions and deletions will undoubtedly occur within a very short time; nevertheless, this approach is being presented now because there appears to be a need for information on the technique of this very delicate and complex surgical procedure within the human temporal bone.

This is not simple surgery. Experience seems to indicate that this procedure in its present early form should be limited to the otologic surgeon who is skilled in fenestration surgery, for two reasons: *1.* He has the specific anatomical training and surgical dexterity necessary for intra-tympanic manipulations. *2.* The patient who is subjected to a stapes procedure is entitled to have available to him the fenestration operation, if the stapes procedure is unsuccessful. It is not logical that a patient be required to seek surgical help through fenestration at the hands of another surgeon if the stapes footplate cannot be mobilized.

When the stapedolysis procedure is successful, the advantages to the patient are important. Because of the preservation of the functioning tympanic membrane and ossicular chain, the hearing restoration is usually excellent. The surgical procedure is much simpler for the patient, from the point of view of short hospitalization, simple and brief postoperative course, relative absence of side effects and discomfort.

TECHNIQUE.

1. Preoperative Care.

The preoperative medication for stapedolysis surgery should not be heavy. It should be sufficient to produce a calm entry into the operating room but not deep enough to obtund accurate responses for audiometric threshold studies. The patient should be slightly sleepy but not heavily narcotized. For this purpose, barbiturates alone usually suffice. Three grains of sodium pentobarbital are usually sufficient for this procedure; this medication is given in divided doses about two hours and one hour before surgery. Morphine and its analogues are usually not used. There is no need for atropine or similar drugs.

2. Preparation.

Hair preparation is kept at a minimum. The hair is not shaved but is usually kept out of the surgical field by the use of a modified bathing cap or adhesive tape. The head is placed with the opposite ear in a comfortable doughnut retainer, and the patient is asked to hold a push button for use in audiometric responses, and is instructed in the audiometric technique to be employed. Usually, the same audiologic technician who examined the patient preoperatively does the operative audiometry.

The peri-auricular area and the auricle are cleansed in the usual manner as for any surgical procedure. Cerumen, dead epithelium and crusts are carefully removed from the external auditory canal by the surgeon; the canal is filled with a 1-1000 aqueous zephiran solution, and a trailer quarter-inch gauze is packed into the canal, completely covering the tympanic membrane.

The purpose of this aqueous zephiran preparation is twofold: *a.* It is designed for antiseptic preparation; *b.* It serves to create some edema of the tympanic membrane. This is important inasmuch as some tympanic membranes are parchment-like and atrophic in their consistency; such tympanic membranes are very easily ruptured in the surgical exposure of the middle ear. Preliminary contact of 15 to 20 minutes

with aqueous zephiran solution creates sufficient edema in the epithelial layers of the tympanic membrane to permit easier elevation, with little danger of perforation.

3. Anesthesia.

The cutaneous lining of the bony canal wall is adequately anesthetized by blocking with a mixture of 2 per cent xylocaine, three parts, and 1-1000 adrenalin, one part, following Rosen's[8] recommendation. A total of less than 1 cc. of this mixture is needed for adequate local anesthesia of the entire cutaneous bony canal lining and the tympanic membrane. The anesthesia solution is injected with a 3-inch 22-gauge short beveled needle at the four points of the circumference of the external canal, at the junction of the bony and cartilaginous canal walls.

The solution is allowed to dissect the subcutaneous tissue down towards the annular sulcus region. Pressure is applied by means of small saline cotton balls to encourage subcutaneous dissection by the anesthesia solution medially, so that partial elevation of the annular flap is achieved.

4. Incision.

The incision in the posterior half of the canal skin is omega shaped, starting superiorly at about the junction between the pars tensa and pars flaccida and ending at the inferior aspect of the annulus. The apex of the omega is at the lateral extremity of the posterior bony canal wall. The skin is dissected from bone with a slender periosteal elevator (see Fig. 1).

The elevation is facilitated by gentle blunt dissection, using wet cotton applicators. Several suture lines may be present, depending upon the developmental anatomy of the os tympanicus. When these suture lines are reached, they are carefully incised with a sharp knife (blunt dissection at these points should be avoided). This elevation of the dermal-periosteal flap can be accomplished rapidly but should be done with magnification, using a loupe. The elevation is carried medially until the margin of the annular sulcus is reached.

5. Annular Elevation, Opening of Middle Ear, and Exposure of Incudo-stapedial Joint.

When the margin of the tympanic sulcus is reached, a round angulated elevator is used to enucleate the annulus fibrosus from the sulcus. Following the enucleation, penetration of the tympanic air space is accomplished. The enucleation of the fibrous annulus from the sulcus is continued superiorly, and inferiorly, until exposure of the entire posterior half of the middle ear is obtained. This exposure will be limited superiorly by the junction of the pars tensa and pars flaccida.

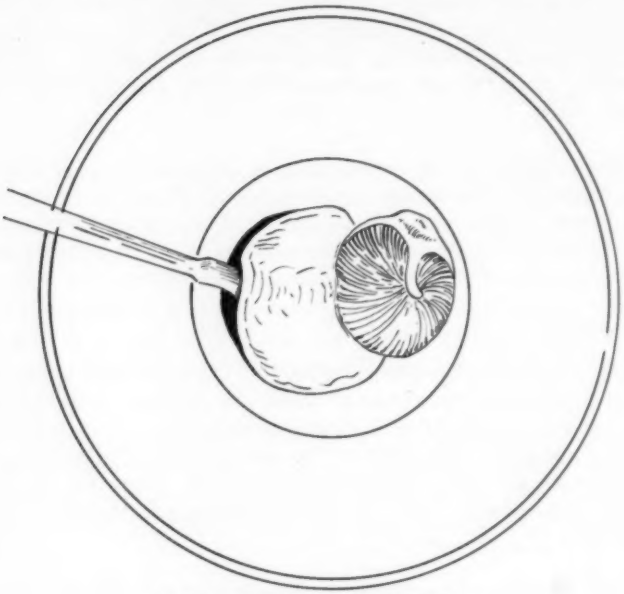

Fig. 1. Elevation of annular flap.

When this exposure is completed (see Fig. 2), in at least 50 per cent of cases a direct view of the entire incudo-stapedial joint will be obtained, along with the chorda tympani nerve, stapedial tendon, part of the posterior stapedial crus and part of the anterior crus. Occasionally the posterior aspect of the handle of the malleus will be seen. The promontory and the round window niche will usually be prominently in the field.

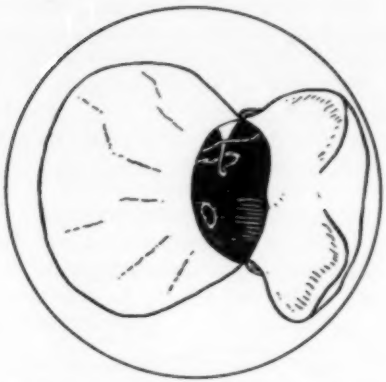

Fig. 2. Excellent exposure of the incudo-stapedial joint.

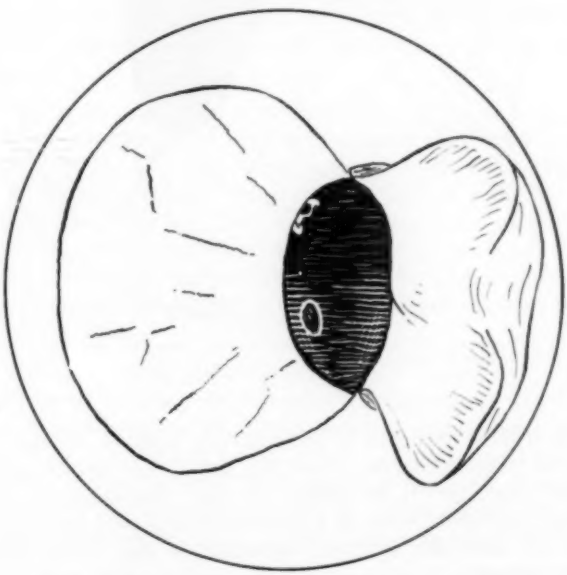

Fig. 3. Poor exposure of the incudo-stapedial joint.

If such a clear visualization is not easily obtained (see Fig. 3), it is necessary to obtain adequate exposure by removal of sufficient postero-superior bony annular quadrant to make this possible. This may be accomplished in some cases by the use of a sharp small curette. In many instances, it can be accomplished only by the use of a small modified Lempert 1 or 2 mm. burnishing burr on a contra-angle dental handpiece (see Fig. 4).

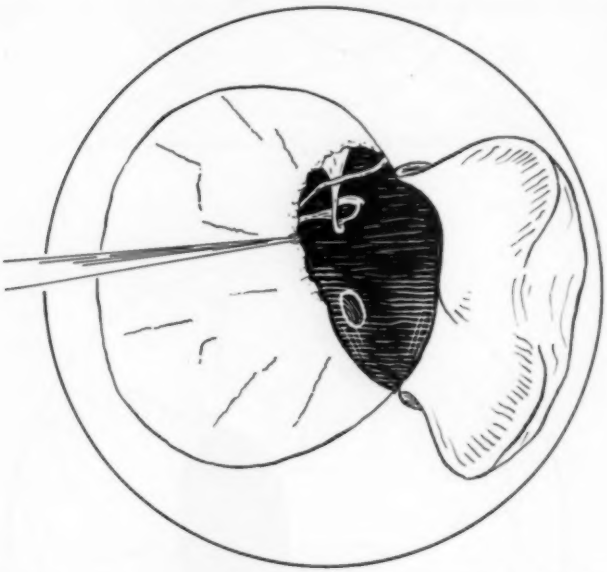

Fig. 4. Removal of bone postero-superior annular quadrant for better exposure of incudo-stapedial joint.

Such bone removal is done gently without trauma to the chorda tympani nerve, which can usually be pushed aside with little difficulty. It is rarely, if ever, necessary to cut this nerve. Sufficient bone in this quadrant should be removed to give an adequate surgical approach to the incudo-stapedial articulation.

6. Operative Audiometric Technique.

It is now necessary to describe the technique of operative audiometry utilized in this procedure, because its employment begins at this point. The audiometric purpose is to obtain comparative threshold levels for guidance in manipulation of the incudo-stapedial joint for stapedolysis. These are relative and not absolute threshold values, such as might be obtained in an adequately sound-treated room. Thresholds are obtained for air conducted sound at frequencies of 500, 1000, 2000 and 4000 cycles without masking of the opposite ear in the reasonably quiet environment of the operating room (without special acoustic treatment).

Surgical procedures are performed at times when extraneous ambient noise levels will be at a minimum; usually in the afternoon when all other operating rooms have been emptied. The doors are kept closed, and extraneous disturbing noises are discouraged by operating room personnel. (Ideally, of course, it would be fine to have available an acoustically treated operating room, but adequate relative studies may be done in an ordinary operating room under the circumstances decribed above.)

Any acceptable and calibrated pure tone audiometer may be used for this purpose. A sterile field cover is draped over the operative field. The audiologist places an air conduction receiver on the covered auricle and it is held in place by a sterile towel (see Fig. 5). The same conditions are used for all four basic steps. Consequently, the attenuation by the sterile field cover is a constant factor, and can be disregarded since the purpose is relative threshold determination for threshold shift only.

Four basic threshold determinations are necessary. (In some instances, as many as six or seven threshold studies might be required during the progression of lysis attempts.) The basic four studies are as follows: *1.* Middle ear closed after initial incision has been made and flap replaced; *2.* Middle ear open*; *3.* Guidance threshold *after* manipulation through incudo-stapedial joint. (This third step may require

* We have noted the frequent occurrence of an improvement in hearing at 4000 cycles when the middle ear is open before stapedolysis.

one or several repetitions to obtain evidence of either lysis or complete ankylosis); *4*. Middle ear closed again (this final step is made as a final estimate of the threshold shift as compared to *Step 1*).

In some instances, it is advisable to employ *Step 4* as an extension of *Step 3*, when the threshold shift with *Step 3* is minimal. Under these circumstances, it may also be informative to repeat *Step 4* several times. In the average case, the minimum of the four steps is adequate; in some cases it is necessary to do more than four studies.

Fig. 5. Illustration of technique for operative audiometry.

7. Microscopic Study of Operative Field and Palpation of the Incudo-stapedial Joint.

At this point in the procedure, it is usually advantageous to bring into use the dissecting microscope, which is a modified Bryan surgical microscope, with the addition of an infrared filter and a condensing lens to concentrate the light beam for use through an ear speculum. It may require considerable manipulation of the position of the patient's head, the position of the speculum, and the angle of the microscope to accomplish adequate visualization of this area; but the advantages to be gained are well worth the slight inconvenience of such prolonged manipulation maneuvers.

The various structures previously enumerated are inspected carefully with the microscope, and special attention is paid to the crura and the region of the stapes footplate. It is not unusual to find pathologic atrophic fractures of the crura before any surgical attack has been directed to this area.

In advanced otosclerosis with osteogenetic destruction of the stapedial footplate it is possible to find that the crura have been pathologically thinned, and actually replaced by fibrous strands in the region of the footplate, which is now no longer an anatomical footplate but a distorted bony area filling the fenestra ovalis, which in itself may demonstrate deformation of its margins.

8. Trans-incudal Manipulation to Produce Stapedial Footplate Lysis.

It was observed on a number of occasions that mobilization of the stapes by the use of force directed toward the neck of the stapes, as described by Rosen,[8] would not infrequently produce immediate disruption of the incudo-stapedial joint. This is to be expected from an analysis of the mechanical forces involved in this procedure.

The incudo-stapedial joint is an enarthrosis, a ball and socket joint with poly-axial motion and no ligamentous limitation. Fenestration surgeons are familiar with ease of disarticulation of the lenticular process of the incus from the head of the stapes; thus, force applied to the stapes neck posteriorly may easily disrupt the incudo-stapedial joint.

I found that it was more feasible to direct the application of force to the incus itself and apply it through the incus to the stapes through the incudo-stapedial joint. It is thus possible in many instances to produce stapedolysis by trans-incudal force without concomitant incudo-stapedial dislocation.

A slightly curved sharp probe is inserted into the periosteal surface of the lenticular process and the integrity of the incudo-stapedial joint judged by palpation (see Fig. 6). If exploratory pressure reveals that it is possible to transmit force to the stapes safely, immediate lysis attempts are made.

If such exploration reveals a very loose incudo-stapedial joint, it is intentionally immobilized by cementing before force is applied (see Fig. 7). Immobilization is accomplished by the use of pentocryl, a fast setting resinous plastic applied in a semi-solid state to the incudo-stapedial joint.

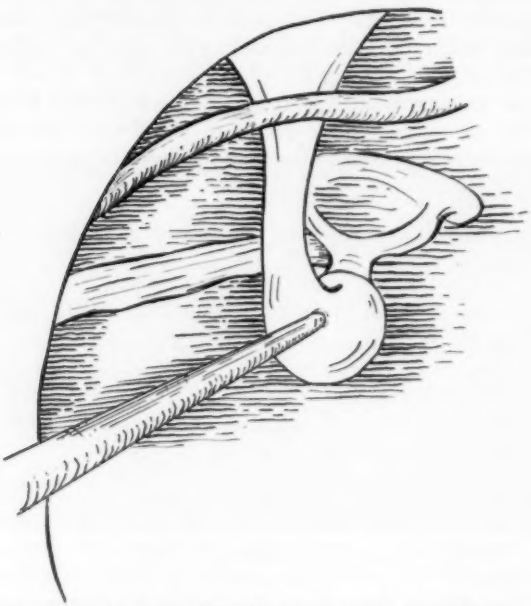

Fig. 6. Trans-incudal mobilization of stapedio-vestibular joint.

When the incudo-stapedial joint appears relatively stable, either naturally or following pentocryl cementation, attention is directed to the stapedial muscle tendon. This usually inserts on the posterior stapedial crus near the neck. If the tendon appears stretched and under tension, a fine angulated knife is passed underneath it at its insertion, and it is cut away from the stapes to prevent counter pull, which might favor either crural fracture or incudo-stapedial joint dislocation.

When it is possible to apply force it is applied through the probe, first in a posterior direction and then in an anterior

direction, occasionally inferiorly and occasionally superiorly, and occasionally in a gently rotatory fashion. Frequently, application of such force in any one of these directions is followed by a slight audible crack and the voluntary statement by the patient that there was a change in auditory threshold.

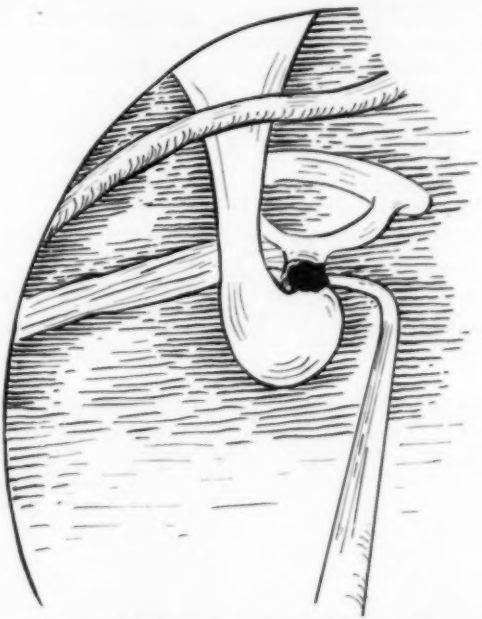

Fig. 7. Cementing of incudo-stapedial joint.

Common expressions made by the patient are, "something just opened up," "I felt something snap," "I felt a loud noise in my ear," etc. At such a point it is desirable to perform *Step 3* of the audiometric study. If this *Step 3* shows an immediate improvement in threshold, the middle ear is closed, and *Step 4* is performed. If the threshold shift is 20 or more decibels in the speech frequencies, it is considered that significant lysis has been accomplished.

If there is no voluntary statement by the patient, *Step 3* is performed after a series of forces have been applied in the

(Case No. 31)

		Air Conduction				Bone Conduction			
		500	1000	2000	4000	500	1000	2000	4000
Preoperative Audiometry:		40	40	35	35	10	15	5	10
Operative Audiometry:	Step 1—Tympanum closed	50	45	40	50				
	Step 2—Tympanum open	60	60	40	30				
	Step 3—Tympanum open (after stapedolysis)	45	35	25	25				
	Step 4—Tympanum closed	25	25	35	55				
Postoperative Audiometry:	2 weeks after surgery	30	25	25	25				

Fig. 8. Operative Audiometry Chart. This illustrates a typical successful stapedolysis record. Steps 1, 2, 3 and 4 illustrate the thresholds obtained under conditions described in the text.

(Case No. 51)

		Air Conduction				Bone Conduction			
		500	1000	2000	4000	500	1000	2000	4000
Preoperative Audiometry:		70	70	70	80	35	45	25	45
Operative Audiometry:	Step 1—Tympanum closed	65	75	80	80				
	Step 2—Tympanum open	65	80	80	90				
	Step 3—Tympanum open (after attempted stapedolysis)	65	80	75	85				
	Step 4—Tympanum closed	70	80	75	85				
Postoperative Audiometry:	2 weeks after surgery	60	65	65	75				

Fig. 9. Operative Audiometry Chart: This illustrates a typical unsuccessful stapedolysis record in a poor candidate (note bone conduction). Steps 1, 2, 3, and 4 illustrate the thresholds obtained under conditions described in text.

various directions mentioned. These forces are of very small magnitude, and are gently applied with every effort not to disrupt the incudo-stapedial articulation. If operative audiometric *Step 3* shows no significant threshold shift with probe manipulation, it may be assumed that the ankylosis is of major degree (see Figs. 8 and 9).

It was found that under such circumstances it was possible to produce lysis by mechanical rapid vibratory force if the continuity of the stapedio-vestibular articulation had not been destroyed by the otosclerotic process. If observation with the dissecting microscope reveals severe pathologic crural or footplate changes, further manipulation is discontinued, and the operation is concluded.

9. Use of the Microvibrator in Trans-incudal Stapedolysis.

A microvibrator was devised, utilizing a dental handpiece with an "amalpak" automatic hammer attachment, to which was added an offset right angle probe to transmit hammer-like forces to the incus (see Fig. 10). The rate of motion of the

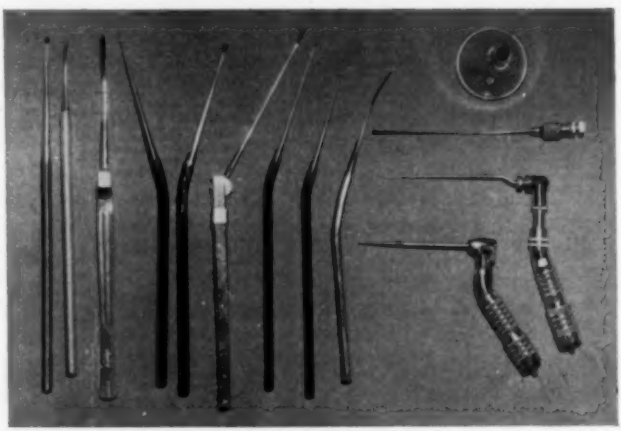

Fig. 10. Instruments Used: Basic instruments used in stapedolysis. A variety of bone elevators, probes and scalpels are needed for the dissection and for manipulative purposes.

a. Illustrates the contra angle attachment to the dental handpiece for the use of a specially grooved burnishing burr.

b. Illustrates an automatic hammer attachment to the dental handpiece with an offset probe which constitutes the microvibrator described in the text.

vibrator is controlled by the foot control of the dental engine in the same manner as in the use of the burr. The microvibrator probe is applied to the lenticular process of the incus. The amplitude of motion of the microvibrator is less than 0.5 mm. Exploratory bursts of vibration are utilized in varying speeds, and results are observed visually and studied audiometrically.

If use of the microvibrator in all four direction using varying speeds is not followed by an appreciable threshold shift, on *Step 3* audiometric run, the procedure is concluded with the assumption that the footplate region is ankylosed beyond the possibility of lysis by current surgical techniques.

10. Closure of Incision.

When a decision has been made as to the status of the stapediovestibular joint, the drum and skin flap are replaced closing the middle ear.

11. Dressing.

Upon replacement and final *Step 4,* audiometric evaluation, the wound edges are carefully approximated to their preoperative positions and covered by strips of rayon gauze saturated in saline. All of the raw areas are covered, as is the entire tympanic membrane. A cylindrical piece of nylon wool is impregnated with neomycin hydrocortisone "acetate F" ointment and placed within the lumen of the external auditory canal, and against the tympanic membrane, with concentric pressure against the rayon saline strips. Two or three such pledgets are inserted into the external auditory canal to apply evenly distributed pressure in all directions. A dry cotton plug is inserted as a final dressing to close the meatus. No head dressing is deemed necessary.

12. Postoperative Care.

A. Pain. There is slight pain following this surgical procedure, but it is relieved by the use of aspirin, codein or demerol.

B. Ambulation. The patient is allowed to be ambulatory as soon as the effects of the barbiturate medication have worn off.

C. Antibiotics. Prophylactically, tetracycline 250 mgm. four times a day for five days. In patients sensitive to the mycin drugs, other suitable antibiotics or sulfonamides may be administered.

D. Vertigo. Some patients will experience immediate slight or moderate vertigo, and in some instances nystagmus may be observed. Such vertigo is usually self limited within a few hours. If it is annoying, it may be alleviated by small doses of dramamine by mouth, occasionally by injection.

E. Hearing. The hearing level in the operated ear, which may be elevated at the time of surgery, usually drops in the postoperative period and may remain unchanged, or even lower than the pre-operative level, for the first five to seven days. In many successful lysis cases, the Rinné test remained negative for seven to ten days following surgery, and then became positive.

F. Packing Removal. The dressing is removed gently on the seventh day. If slight bleeding occurs, the wound is re-packed and not disturbed for another five days, after which it is usually simple to remove.

When the packing has been completely removed, it will usually be observed that the flap is well healed, the tympanic membrane appears mobile and in most instances is translucent. Hemotympanum and serous effusion are encountered only rarely postoperatively and usually subside spontaneously. No further dressing is employed after the packing has been removed. It is rarely necessary to treat the canal with any type of medication.

SUMMARY.

A method has been described for the purpose of mobilization of the stapes by the technique of trans-incudal stapedolysis. This new technique has been found effective in increasing the number of good results following this type of surgery.

Special features of this technique include: *1.* Trans-incudal application of force; *2.* Operative audiometric control; *3.* Use of a mechanized microvibrator, and *4.* Prevention of incudostapedial dislocation by cementing.

It is too early at this stage to report on results of such surgery, but such reports are planned when sufficient time has elapsed to warrant long range evaluation.

The experience to date indicates that this may be a very useful procedure in an unknown percentage of otosclerotic patients. In suitable cases, if the procedure produces long range results, it has many advantages over fenestration of the semicircular canal. If irreversible footplate disease prevents stapedolysis, this technique will not prevent the possibility of a successful fenestration operation later.

By no means does this procedure replace fenestration in the surgery of otosclerosis. It is an added technique to the armamentarium of experienced otologic fenestration surgeons who are equipped by training and experience to do the delicate manipulations in this field and who can offer their patients a complete surgical rehabilitation program, so that if the stapedolysis procedure is not effective, fenestration may still be effective in surgical restoration of hearing.

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AUDITORY FUNCTION AS RELATED TO THE COMPLAINT OF DIZZINESS.

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Disturbances of the vestibular complex may excite such postural confusion and physical incapacity that the relatively less impressive sensation of hearing impairment may be temporarily unnoticed, especially during the initial stages of affliction. The auditory segment of the temporal bone is normally the most sensitive but also the least resistant to a variety of insults; hence its functional integrity contains the diagnostic, prognostic and therapeutic key to a number of clinical symptoms associated with what the patient describes as dizziness. It is up to the examiner to differentiate between labyrinthine vertigo and other types of postural or locomotor instability which may be called dizziness.

Dizziness is a common complaint encountered in the practice of medicine and its connotations excite a multiplicity of diagnostic considerations which necessitate a series of complex and time-consuming examination procedures. The most essential of these, after securing an accurate and detailed description of the patient's symptoms, is the auditory survey preferably preceded by the otoscopic examination. The otoneurologic examination should include routinely the differential caloric tests subsequent to a painstaking search for spontaneous or positional nystagmus.

The information thus obtained along with that of the remaining neurologic examination, X-rays of the internal auditory meatuses and ophthalmoscopic investigations[1] will facilitate a differentiation between peripheral and central types of dizziness upon which one may place relatively high diagnostic value.

There are few audiometric patterns which of themselves are

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typical or characteristic of specific etiology; however, tympanic and inner ear types of hearing loss can be identified, and evidence is accumulating that may make it possible to distinguish between at least two types of inner ear hearing loss.[2] It is essential that the acuity of hearing for both air and bone conduction be determined in order to learn where to focus the search for the etiology of dizziness.

Nearly all peripheral vestibular disturbances are accompanied by hearing loss, although there are a few exceptions which will be discussed presently. Hearing loss is less frequently associated with central causes of dizziness, but in some cases it is the primary and cardinal symptom.

Recruitment and threshold fatigue are peculiar phenomena of hearing which may be helpful in differentiating between cochlear and neural lesions.[3,4,5] Recruitment may be defined as an abnormally rapid appreciation of loudness as the intensity of a given sound is gradually increased. The Bèkésy type audiogram reveals this in the short excursions made by the recording pen which is actuated by the patient's signal response to pure tone threshold stimulation.

Dix, Hallpike and Hood[6] noted that recruitment characterized hearing impairment of cochlear origin, as in labyrinthine hydrops, but that it did not accompany hearing loss of a neural nature, such as occurs from compression of the auditory nerve by acoustic neuromas.

Auditory threshold fatigue may be defined as a decrease in threshold sensitivity resulting from successive exposures to sound which can just barely be heard. Excessive fatigue at threshold has been reported as a significant finding in neural types of deafness but not present in cochlear hearing loss. Reger and Kos[7] have noted temporary threshold fatigue in cases of acoustic neuroma and atrophy of the acoustic nerve. Sufficient evidence has not yet accumulated to the extent that the interpretation of these observations may be accepted with complete confidence; however, they may be looked upon as potentially valuable diagnostic expressions of dysfunction which deserve exhaustive investigation.

It is apparent that regardless of the initial causes these

disturbances may be attributable to circulatory deficiencies due to vasomotor irregularities, nutritional insufficiency, or vascular occlusion. The ultimate effect is an excitatory or degenerative activity extended to the functional segments of the temporal bone.

In those instances in which the dizziness does not indicate or suggest serious consequences to life and for which no exact cause may be readily ascribed, either by otoscopic examination or neurologic evidence of disease, a complement of symptoms comprised of vertigo, tinnitus, hearing loss, nystagmus, and the associated autonomic phenomena is generally recognized as Meniere's Symptom Complex.[8]

There are variations of this complex which regularly trace a symptomatic pattern suggesting an acceptable operational classification for diagnosis, prognosis and treatment that the expression Meniere's symptom complex does not clearly define.[9]

LABYRINTHINE HYDROPS.

The dizziness of labyrinthine hydrops (Meniere's disease) is a spontaneous rotating or spinning sensation, sudden in onset and aggravated by motion, which lasts from a few minutes to several hours. The victim remains conscious and afterwards is usually able to give a detailed account of the attack; however, in some instances, the patient is so terrified and preoccupied with efforts to maintain balance that some essential features of the experience may escape his detection.

Its spontaneous, paroxysmal course is punctuated by varying intervals of well being, during which the general sensory and motor functions seem to be normal except for residual hearing impairment and tinnitus.

The hearing loss is of the inner ear type usually unilateral, and early in the disease involves principally the low tones. Eventually the hearing for all frequencies may be depressed. One of the characteristics of labyrinthine hydrops is the fluctuation of hearing acuity during its initial phases.

If the hearing loss is limited to frequencies below 1000 cycles and does not exceed 20-30 decibels, it may return to normal; otherwise, recurrent attacks apparently introduce the

effects of chronic ischemia, with accompanying deterioration for high frequenices and a permanent residual hearing impairment. Frequently an aura of impending attack is felt as a building up of "pressure in the ears" which is relieved following an attack. Occasionally this relationship is reversed.

Attacks vary considerably in duration, intensity and frequency from individual to individual, and they may occur for a period of several years without severe deterioration of the cochlear function. A relatively rare variation, however, is one having a rapidly progressive course followed by complete destruction of hearing. Paroxysmal dizziness may occur without evidence of hearing loss, and, contrariwise, at least temporarily a fluctuating inner ear deafness may occur without vertigo. Such episodes usually eventuate in the more familiar

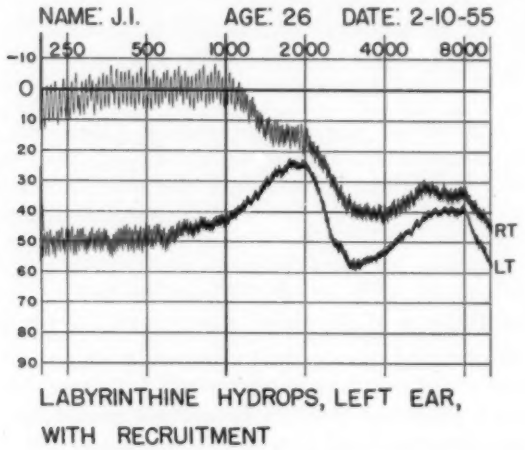


Fig. 1. The narrow swings indicate recruitment.

combination of effects. Tinnitus is often described as a roaring, buzzing, or sizzling noise in the ear. Its intensity rises and falls in some relation to the sensation of dizziness.

Recruitment is observed audiometrically. Usually it is not marked unless the hearing loss exceeds 30 decibels, and it is more severe for higher frequencies than for low (see Figs. 1

and 2). In some patients, recruitment subsequently disappears, possibly because of the effects of chronic ischemia on the auditory nerve (see Fig. 3).

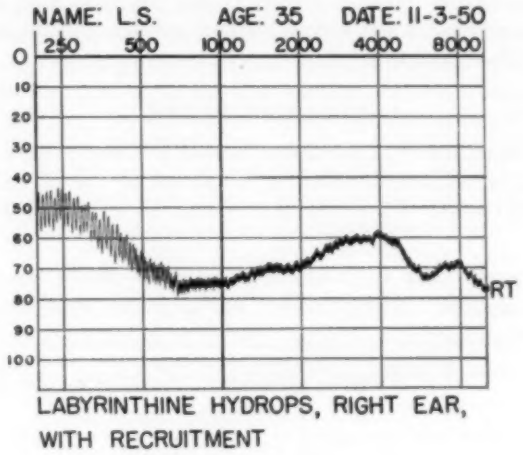


Fig. 2.

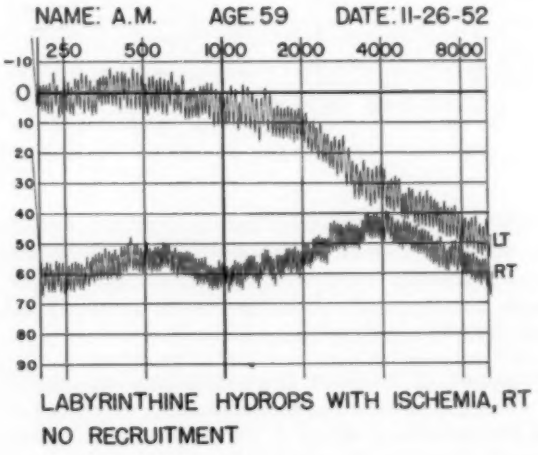


Fig. 3.

Threshold fatigue is not characteristic of labyrinthine hydrops, though it may be present to a slight degree in some patients whose attacks have been of several years' duration.

Labyrinthine hydrops affects young adults as well as those of more advanced age, but its highest incidence is among those in the 35-45 age bracket.

LABYRINTHINE ISCHEMIA.

The dizziness of labyrinthine ischemia varies from a partial turning or segmental spinning sensation to one of oscillation and uncertainty of posture or position. This is a degenerative

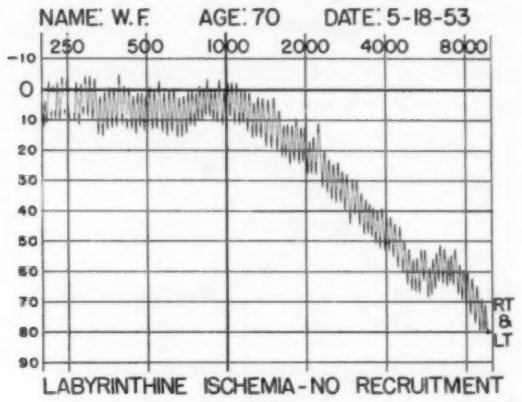


Fig. 4.

process. The dizziness occurs, not as distinct, spontaneous episodes, but rather as superimposed exacerbations on a persistent unsteadiness or locomotor instability. Quick head movements, sudden postural changes or certain positional attitudes are definite exciting factors.

Intermissions of freedom from dizziness are experienced usually when the patient remains immobile, or when he learns to avoid the positions which bring on the discomfort. The slightest change in position is likely to initiate a sensation of

falling which lasts a few seconds to a few minutes, or may be prolonged for hours.

A carefully taken history and painstaking inquiry will often reveal that labyrinthine ischemia is influenced by diurnal physical activity. One patient may complain that dizziness is worse in the morning but recedes after a few hours of moving about. Strong coffee is usually his favorite beverage, and several cups may be consumed before he feels like indulging in much activity. Another may complain that his dizziness is worse in the afternoon or evening, during which he tires easily from normal activities. These are important clues to therapeutic management and symptomatic prognosis.

The hearing loss, as distinguished from that observed in labyrinthine hydrops, is of the high frequency, inner ear type, and may or may not exhibit recruitment, presumably depending upon whether the end-organ or nerve is primarily affected (see Fig 4). It is usually bilateral.

Hearing never fluctuates, but progressively deteriorates. The tinnitus is described as whistling, ringing or squeaking, and sometimes is compared to the sound of a ricocheting bullet. Some of these patients show evidence of auditory threshold fatigue in the absence of recruitment which suggests nerve involvement. One patient who did not reveal a recruitment response, but rather severe fatigue at threshold, was observed to have marked atrophy of the auditory nerve during an exploratory exposure which was done because she was suspected of having an acoustic neuroma (see Figs. 5A and 5B).

This clinical picture indicates a slowly progressive disintegration of reflexes because the circulation provides less and less of the nutritive elements necessary to maintain efficient and effective labyrinthine activity. There is no significant correlation in the finding of vascular hypertension or hypotension as the cause of this dizziness, but arteriosclerosis is a commonly associated condition.

The period of life in which this type of dizziness more frequently appears is the one upwards of 45 years of age.

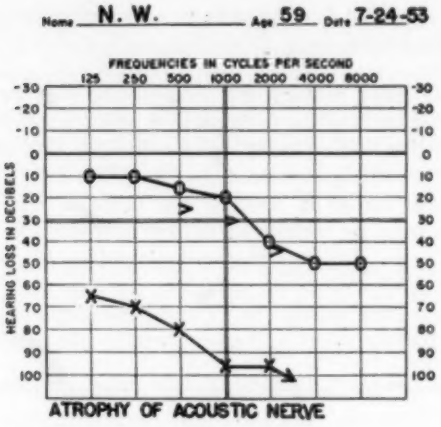

Name N. W. Age 59 Date 7-24-53
FREQUENCIES IN CYCLES PER SECOND
125 250 500 1000 2000 4000 8000
HEARING LOSS IN DECIBELS
-30 -20 -10 0 10 20 30 40 50 60 70 80 90 100
ATROPHY OF ACOUSTIC NERVE

Fig. 5A. Pure tone clinical audiogram showing severe impairment of hearing in the left ear. Note the threshold of hearing at 500, 1000, and 2000 frequencies for comparison with Figure 5B.

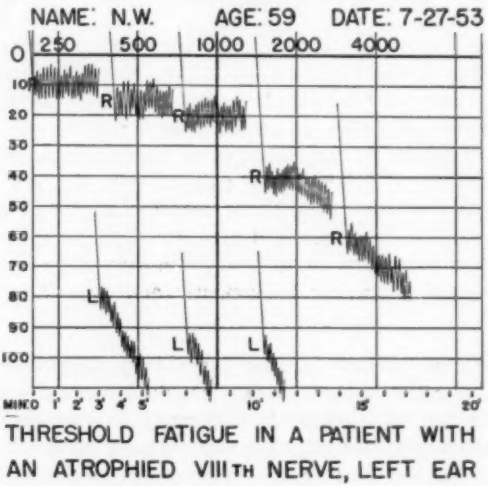

NAME: N.W. AGE: 59 DATE: 7-27-53
250 500 1000 2000 4000
0 10 20 30 40 50 60 70 80 90 100
R
L
MINS 1' 2' 3' 4' 5' 10' 15' 20'
THRESHOLD FATIGUE IN A PATIENT WITH
AN ATROPHIED VIII TH NERVE, LEFT EAR

Fig. 5B. Threshold recordings with the Bekesy type audiometer shows threshold shift in left ear at 500 cps from 80 db to 110 db in about two minutes; at 1000 cps from 95 db to 110 db in about one minute; at 2000 cps from 95 db to 110 db in less than one minute. Note this shift does not occur in the right ear except slightly at 2000 and 4000 cps. This audiogram differs from those previously shown in that the threshold was obtained at fixed frequency levels as is done in pure tone clinical audiometry, i.e., the test frequency remains constant.

LABYRINTHINE APOPLEXY.

Acute labyrinthine anoxia, such as occurs as the result of labyrinthine ablation, vascular occlusion or severe, prolonged vasospasm, is often difficult to differentiate initially from a severe episode of labyrinthine hydrops; however, the nature of the disturbance is eventually established by the persistence and intensity of both subjective and objective symptoms. The dizziness is a true vertigo, and its duration is several weeks during which time there is gradual improvement. Depending upon the physiological age of the patient, varying degrees of recovery from dizziness take place. Vertigo and the tendency to sway persist longer in elderly people and may never cease. The older the patient the less likely complete compensation will occur. Young adults recover somewhat more rapidly and completely.

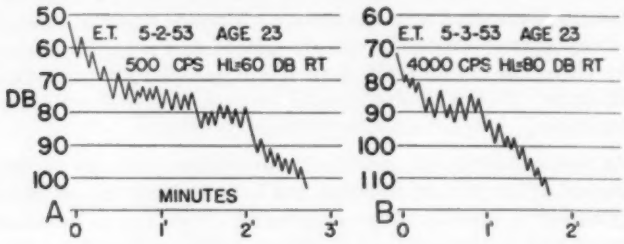
In some individuals, vestibular excitation may be partially restored after several months, but hearing loss which is usually severe is permanently established. Tinnitus is invariably present and is high pitched. Isolated insults may offend either the cochlear or vestibular organ separately. The hearing loss when present is unilateral. During the past ten years several young adults have been observed who sustained vestibular apoplexy without impairment of hearing.

Recruitment is not of diagnostic significance in labyrinthine apoplexy as the hearing loss is usually too severe to obtain reliable measurements; however, when hearing is measureable recruitment may not be present.

ACOUSTIC NEUROMA.

Hearing impairment is the most frequent initial symptom of acoustic neuroma which also causes dizziness.[10] These patients usually are seen first by the otolaryngologist who, unless he conducts a very meticulous neuro-otologic examination, is apt to overlook the true significance of the hearing loss. There is nothing characteristic about the pure tone audiometric test results except that they denote a non-middle ear type of impairment and that recruitment is absent. Threshold fatigue is notably present (see Fig. 6). These findings associated with the other familiar signs and symptoms which appear in acoustic neuroma have appreciable diagnostic value.

Rarely midline brain tumors give rise to discrepancies in hearing as an initial clue. In a case of pinealoma the earliest symptoms were dizziness and difficulty in understanding speech. Parodoxically hearing for interrupted pure tones as tested with a clinical audiometer was normal. The patient was immediately suspected of malingering, but this consideration was soon dispelled when it was found that the Bèkésy automatic stepless intensity type of test showed rapid threshold fatigue without evidence of recruitment.



THRESHOLD FATIGUE IN A PATIENT WITH AN ACOUSTIC NEUROMA

Fig. 6A and 6B. Threshold fatigue at 500 cps from 60 db to 100 db in two minutes, 45 seconds; at 4000 cps from 80 db to 110 db in one, 45 seconds.

Speech discrimination tests revealed very poor appreciation responses, but this alone may not be considered diagnostically significant of a central lesion. In a matter of a few weeks papilledema and subsequent exploratory surgery confirmed the suspicion of intracranial involvement. As the result of palliative surgery the patient has recovered his full powers of hearing, no longer shows threshold fatigue on the Bèkésy test, and is currently being observed for eventual changes which are expected to occur.

Multiple sclerosis early in its course may give rise to differential diagnostic speculation. Hearing loss is usually slight if present, but vertigo may be severe. Recruitment does not occur but excessive fatigue at threshold may be exhibited.

These are only a few of the clinical perplexities of which alterations in hearing may provide the key to earlier and

more accurate diagnosis. Despite the protests that accurate hearing tests may be inconvenient or difficult to obtain, audiometry and audiology are essential to those who undertake the responsibilities of managing the complaints of otologic origin or expression such as dizziness.

CONCLUSION.

Auditory symptoms associated with dizziness may be overlooked by both patient and physician because of their respective preoccupation with the relatively more alarming symptom of dizziness.

Auditory impairment and some of the peculiarities associated with it (*e.g*, recruitment, threshold fatigue) often are helpful in determining the general area of insult.

Auditory impairment for pure tones may trace suggestive patterns which when correlated with the results of a thorough examination lend considerable support to reliable diagnosis.

Auditory function is frequently the important clue to the definition of dizziness.

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SECRETORY OTITIS MEDIA REQUIRING MASTOIDECTOMY.

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Although it is extremely unusual for secretory otitis media to require mastoidectomy, the procedure has been recorded.[1]

The patient was a white woman of 40, in good health and with no past history of note. She had had no ear trouble nor allergies.

A week before being seen in my office, she had had a nosebleed (no other history of nasal trouble of any kind). Her nose was packed by another doctor. This stopped the bleeding, but caused her to have pain in the ear on that side (left). There was no post nasal pack. The pain remained after the packing was removed. The doctor told her that her ear was normal despite the pain. When she came to me the pain had subsided, but in its place was a most distressing full feeling and tinnitus. She did not complain of hearing loss.

Examination showed no demonstrable upper respiratory infection or sinusitis, nor were her membranes allergic looking. The right ear drum was normal. The left ear drum was slightly full, had a yellow cast inferiorly and was immobile. The eustachian tube was catheterized under direct vision. Air bubbles were then seen through the drum. A myringotomy was done and clear, moderately thick, yellow fluid was obtained. The symptoms as noted above disappeared at once. The ear drained for two days. During this time there were no disturbing symptoms.

On healing (third day), the symptoms returned. The left eustachian tube was again catheterized, and air bubbles were again seen; but there was no relief from her symptoms. A few days later another myringotomy was done, again with immediate relief. A culture and smear of the fluid was taken. The smear was negative, no cells whatsoever were seen. The culture showed pseudomonas aeruginosa, which was moderately sensitive to Terramycin. This was given, 500 mg. t.i.d. for ten days, and also Terramycin ear drops. No relief was obtained.

Several subsequent myringotomies were then performed with similar results, *i.e.*, complete relief from symptoms while the ear drained (usually two to three days), and return of symptoms on healing. A second culture was negative. On several occasions it was noted that more fluid was obtained than the middle ear could possibly hold. The character of the fluid remained as described above. Subsequent smears were negative.

Allergic tests were performed. They were negative; nevertheless, antihistamine therapy was tried, but without success. Radium was then applied to the nasopharynx, again without success.

Audiometric and fork tests (repeated) showed the following: Right ear was normal, left ear normal bone conduction, but air conduction varied between a 30 to 40 decibel loss throughout the frequencies. Fork

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tests showed bone conduction greater than air conduction on the left, and the Weber lateralized to the left.

After several more myringotomies (four months after the onset) a very large incision was made in the drum and a polyethylene tube inserted as described by Armstrong.[2] This was left in place for three weeks. During this time the patient was happy and symptom free; however, upon removing the tube, the drum healed and all symptoms returned. Thyroid extract, by mouth, was tried without success.

A mastoid X-ray was then taken. It showed localized changes suggesting a chronic osteotitis. Mainly because of the distressing symptoms a simple mastoidectomy was performed. This was eight months after the onset of the disease. The following was found: clear amber fluid welled up to the surface as soon as the perforating drill was withdrawn.

On removing the cortex, there was seen to be bone softening and cellular destruction near the antrum. Pink fibrous tissue was also present in this area and covered the incus, head and neck of the malleus, semicircular canal and surrounding bone. It had to be scraped off to expose these structures. It also was seen protruding from the middle ear. The mastoid cells distant from the antral region were normal.

A complete simple mastoidectomy was done, including the removal of as much of the fibrous tissue from the middle ear as was possible without dislocating the ossicles. This fibrous infiltration in the antibiotic era mastoiditis was described by Tamari and Szanto in their histopathological studies.[3]

Hotchkiss[1] performed a mastoidectomy for secretory otitis. He found much fluid in the mastoid cells, but no bony destruction or fibrous tissue infiltration. He was "impressed with the normalcy of the mastoid structures."[4]

Post-operatively the disturbing symptoms were relieved and have continued so to the present (five months after operation). The wound drained for seven weeks, then became dry.

Although she does not, nor ever did complain of hearing loss, her hearing is not improved.

CONCLUSION.

Mastoidectomy for secretory otitis media is most unusual. In this case the procedure accomplished what was urgently desired by the patient: relief from her very distressing fullness and tinnitus; but it did not restore her hearing. Undoubtedly, the reason for the hearing loss was the presence of fibrous tissue in the middle ear. The thought arises: would the hearing loss have been prevented by a mastoidectomy early in the disease? More study will be required to determine when and if such surgery should be performed in cases of secretory otitis media.

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3. Tamari, M. J., and Szanto, P. B.: Morphologic Changes in the Mastoid Bone Under Antibiotic Therapy. *Arch. Otol.*, 60:133-140, Aug., 1954.

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1 Summit St.

UNIVERSITY OF ILLINOIS ANNUAL ASSEMBLY IN OTOLARYNGOLOGY.

The Department of Otolaryngology, University of Illinois College of Medicine, announces its Annual Assembly of Otolaryngology from September 19 through October 1, 1955. This Assembly will consist of two parts:

Part I — September 19 through September 24, 1955, will be devoted to surgical anatomy of the head and neck, fundamental principles of neck surgery and histopathology of the ear, nose and throat. This week will be under the personal direction of Maurice F. Snitman, M.D.

Part II — September 26 through October 1, 1955, will be devoted entirely to lectures and panel discussion of advancements in otolaryngology. The chairman of this section will be Emaneul M. Skolnik, M.D.

Registration is optional for one or both weeks. For further information, address Dr. Francis L. Lederer, 1853 West Polk St., Chicago 13, Ill.

POST-GRADUATE COURSES AT TEMPLE UNIVERSITY.

The following Post-Graduate Courses to be given in this Department during the current year:

Post-Graduate Course in Broncho-Esophagology, October 17 - 28, 1955.

Post-Graduate Course in Laryngology and Laryngeal Surgery, September 19 - 30, 1955.

These courses are all to be given in the Department of Laryngology and Broncho-esophagology, Temple University Hospital and School of Medicine, under the direction of Dr. Chevalier L. Jackson and Dr. Charles M. Norris. The tuition fee for each course is $250.00. Further information and application blanks can be obtained from Dr. Chevalier L. Jackson, 3401 N. Broad Street, Philadelphia 40, Pennsylvania.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY.

Plans have been completed for a joint meeting of the North Carolina Eye, Ear, Nose and Throat Society and the South Carolina Society of Ophthalmology and Otolaryngology at Columbia, S. C., on September 12, 13, and 14, 1955. Headquarters will be the Columbia Hotel.

The following ophthalmologists will be on the program: Dr. E. W. D. Norton of New York, Dr. Frank Carroll of New York, and Dr. William B. Clark of New Orleans.

A most attractive program has been arranged. For further information address Roderick Macdonald, M.D., Secretary and Treasurer, 330 East Main Street, Rock Hill, S. C.

SOUTH AFRICAN LOGOPEDIC SOCIETY.

The South African Logopedic Society (Society of Speech Therapists) publishes a Journal in May and October of each year. Articles deal with the organic and psychological aspects of speech defects, and include subject matter of interest to the medical and allied professions.

Relevant contributions in the field of otolaryngology are invited.

Subscriptions are 10/– per annum including postage and should be addressed to: The Editor, Journal of the S. A. Logopedic Society, Witwatersrand University, Milner Park, Johannesburg, So. Africa.

THE AMERICAN OTORHINOLOGIC SOCIETY FOR PLASTIC SURGERY, Inc.

A short course on Plastic Surgery of the Head and Neck will be given by The American Otorhinologic Society for Plastic Surgery at the Morrison Hotel, Chicago, Illinois, extending from October 7 to October 9, 1955, inclusive. For details write Dr. Louis J. Feit, 66 Park Avenue, New York, N. Y.

SECOND GRADUATE COURSE IN PLASTIC SURGERY OF THE HEAD AND NECK

American Otorhinologic Society For Plastic Surgery
October 7th to 9th, 1955 inclusive
at the Morrison Hotel, Chicago, Illinois

An intensive course in Plastic Surgery of the Head and Neck will be given at Morrison Hotel, Clark and Madison Streets, Chicago, Illinois, from October 7 - 9 inclusive, 1955.

The course will be conducted by a faculty of outstanding specialists in this field and will be limited as to the number of participants and to recognized surgeons specializing exclusively in Otolaryngology and Ophthalmology and Plastic Surgery of the Head and Neck as set forth in the Directory of the American Medical Association. For further information address Louis Joel Feit, M.D., Secretary, 66 Park Ave., New York 16, N. Y.

53rd CONGRES FRANCAIS d'OTO-RHINO-LARYNGOLOGIE.

The Fifty-third Congrès Francais d'oto-rhino-laryngologie will be held Octobre 17-22, 1955 in the Grand Amphithéâtre of the Faculté de Médecine, Paris, under the présidency of Mr. le Professeur A. Aubin of Paris, and honorary president Mr. le Professeur Léon Binet, member of the Institute, Doyen of the Faculté de Médecine of Paris.

Numerous communications will be presented and two reports of particular interest will be discussed:

1°) L'otite chronique de l'enfance.
Rapporteurs: MM. BOURDIAL, DEBAIN, COUSSIEU, avec la collaboration d'Yves LALLEMANT (Paris).

2°) La déglutition et ses troubles.
Rapporteurs: MM. MOUNIER-KUHN (Lyon) et A. SOULAS (Paris).

There will also be an exhibit of surgical instruments and other armamentarium of interest to otorhinolaryngologists. For further information address Mr. Raimon, 17 rue de Buci, DANton 55-24.

"SEGUNDO CONGRESO PANAMERICANO DEL CONGRESO INTERNACIONAL DE CIRUJIANOS Y OCTAVAS JORNADAS ARGENTINAS DE CIRUGIA TORACICA"

1. Segundo Congreso Panamericano del Congreso Internacional de Cirujianos — Mendoza (Republica Argentina), 22-26 Octubre, 1955 .

   Bocio: Tratamiento médico y quirurgico.

   Absceso Del Pulmon: Tratamientos modernos.

   Cancer Del Recto y Colon Sigmoedes: Tratamiento quirurgico.

   Micosis y Ostesmielitis del Hueso Maxilar.

   Temas Libres: Adelantos recientes en procedimientos y Técnicos para Diagnosis, Radiologia, Endoscopia, Anestesia, Procedimientos y Técnicas quirurgicas, Antibioticos, etc.

2. Octavas Jornadas Argentinas de Cirugia Toracica — Mendoza (Republica Argentina), 22-26 Octubre, 1955.

   Absceso de Pulmon: Tratamientos modernos.

   Conducto Arterioso: Tratamientos quirurgicos.

   Endoscopia Peroral: Adelantos recientes.

   Temas Libres: Demonstraciones quirurgicas—Programa de Peliculas Cientificas.

For further inquiries address: Biblioteca Asociacion Medica Argentina, Santa Fé 1171, Buenos Aires, Argentina.

BRONCHOESOPHAGOLOGY COURSE

The next Bronchoesophagology Course to be given by the University of Illinois College of Medicine is scheduled for the period October 24 to November 5, 1955, under the direction of Dr. Paul H. Holinger.

Interested registrants will please write directly to the Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Illinois.

DIRECTORY OF OTOLARYNGOLOGIC SOCIETIES.

(Secretaries of the various societies are requested to keep this information up to date).

AMERICAN OTOLOGICAL SOCIETY.

President: Dr. Wm. J. McNally, 1509 Sherbrooke St., West Montreal 25, Canada.
Vice-President: Dr. John R. Lindsay, 950 E. 59th St., Chicago 37, Ill.
Secretary-Treasurer: Dr. Lawrence R. Boies, 90 S. Ninth St., Minneapolis 2, Minn.
Editor-Librarian: Dr. Henry L. Williams, Mayo Clinic, Rochester, Minn.
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President-Elect: Dr. Percy Ireland, Toronto, Canada.
Secretary: Dr. C. Stewart Nash, 277 Alexander St., Rochester, N. Y.
Meeting: Mount Royal Hotel, Montreal, Canada, May, 1956.

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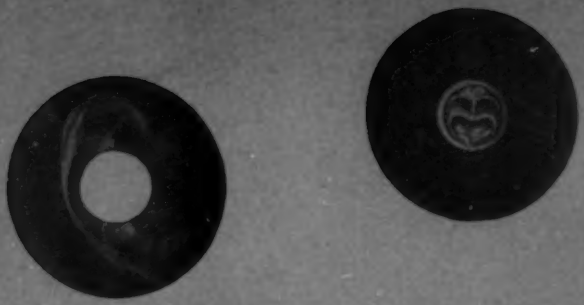
Executive Secretary: Dr. William L. Benedict, Mayo Clinic, Rochester, Minn.
Meeting: Palmer House, Chicago, Ill., October 9-15, 1955.

AMERICAN BRONCHO-ESOPHAGOLOGICAL ASSOCIATION.

President: Dr. Daniel S. Cunning, 115 East 65th St., New York 21, N. Y.
Secretary: Dr. F. Johnson Putney, 1719 Rittenhouse Square, Philadelphia, Pa.
Meeting: Sheraton Mount Royal Hotel, Montreal, Canada, May 15-16, 1956 (afternoons only).

AMERICAN BOARD OF OTOLARYNGOLOGY.

Meeting: Palmer House, Chicago, Ill., October 2-8, 1955.



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